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TRANSACTIONS

OF THE

Mich. Univ. CLINICAL SOCIETY

OF THE

UNIVERSITY OF MICHIGAN

OCTOBER, 1913—OCTOBER, 1914

VOLUME V

EDITED BY THE SECRETARY-TREASURER

FOUNDED NOVEMBER 28, 1902
UNIVERSITY HOSPITAL
ANN ARBOR, MICHIGAN
1914

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VOLUME V.

TRANSACTIONS OF THE CLINICAL SOCIETY OF THE UNIVERSITY OF MICHIGAN

STATED MEETING, OCTOBER 1, 1913

THE PRESIDENT, R. BISHOP CANFIELD, M.D., IN THE CHAIR
REPORTED BY REUBEN PETERSON, M.D., SECRETARY

Reading of Papers

ANNUAL REPORT OF THE SECRETARY-TREASURER FOR THE YEAR 1912-1913.

REUBEN PETERSON, M.D., SECRETARY.

It seems fitting that your Secretary's report should be of a somewhat more formal character this year than has formerly been the custom. For not only does the report cover the tenth year of the Society, since it was founded in 1902 and 1903, but as will be shown, the committee appointed at the last meeting with power to act, has planned a new departure for the Society so far as its transactions are concerned.

Ten years can hardly be said to be a long existence as medical societies go, but this period in the life history of this Society has seen so many changes in the Hospital, with which the Society is so intimately associated, as to make the decade memorable. Like many another medical society, it has had its ups and downs. During the first few years of its existence, at times it languished and seemed about to die. That it did not perish was in part due to the untiring efforts of some of its founders and friends, but principally, I believe, because there has been a distinct need for such a society in our midst. Otherwise it would have gone out of existence long ago.

When Dr. George Dock and your Secretary, planned the new society in 1902, we realized that there were enough regulation medical societies in this community. These societies were well attended, and were doing good work. The new society was to be along different lines, for its underlying idea was the utilization and demonstration of the rich clinical material at the disposal of the members of the University of Michigan Clinical Staff. Set papers were to be avoided unless they had to deal with clinical problems. On the contrary, the members of the various departments of the Hospital, were to be given an opportunity of showing at the meetings of the Society, patients with unusual diseases or complications or where it was impossible to show the patients themselves, to give case reports which were to be followed by comments, deductions and general discussion.

It may be said that this idea, upon which the Society was founded, has been kept constantly in mind throughout the past ten years. Long winded, tiresome, although possibly exceedingly scientific papers, have been conspicuous for their absence. As a regular attendant upon the meetings of the Society for the past ten years, I can bear testimony to the great benefit I personally have derived from the demonstration of cases quite remote from my own field of work, and I feel confident that my own experience coincides with that of other members of the Society.

But apart from what may be learned from the reports of cases, and the demonstration of patients, the founders of this Society had in mind the opportunities such a society would afford the younger men of the Hospital Staff of gaining experience in medical writing, speaking and discussion. There are tricks in all trades, and the trick of clear expression on medical subjects is not born with a man, but must be acquired. With this end in view the heads of the Hospital departments have constantly urged their assistants to make the most of these advantages.

Four years ago the Society, through the aid of the Regents of the University, was able to engage a stenographer, so that the discussions of each meeting might be reported in full. The papers and discussions were published in the *Physician and Surgeon,* and many reprints sent to the physicians of the state and medical alumni. In addition, two hundred and fifty reprints of each meeting were set aside and at the end of the year bound into volumes, which were distributed among the members of the Society, medical libraries throughout the world, and prominent medical alumni. These reprints and volumes have been the means of

placing in medical literature the records of many valuable and interesting cases, which otherwise would have been lost. These volumes have added to the fame of our Hospital and Medical School.

The fourth volume of these transactions is now in press, and will appear shortly. With its publication will cease, for the time being at least, the Society's official connection with the *Physician and Surgeon*, in which journal have been published most of the papers and discussions of the Society for the past ten years. To Dr. John William Keating, the editor of this publication, and former secretary of this Society, the latter owes a great deal, for he has always been its staunch friend. But your committee to whom you referred, at the last meeting, the matter of the Society's transactions, did not feel justified in not accepting the most liberal offer of another journal, especially as the *Physician and Surgeon* did not see its way clear to make any bid for the transactions for the coming year. Your committee, therefore, has selected the JOURNAL OF THE MICHIGAN STATE MEDICAL SOCIETY, as the official organ of the Society. This assures the reports of the meetings being made available to the twenty-four hundred of the JOURNAL'S subscribers each month. At the completion of the Society's year in July or August, two hundred and fifty copies of Volume V, will be bound and distributed as in the past.

It seems fitting that the transactions of the Clinical Society of the State University, should appear in the organ of the State Medical Society, since as citizens and physicans of the state, the members of the State Medical Society ought to be able to keep track of what is being turned out by the men in charge of the Hospital connected with their State University. Also they should have easy access to just the kind of material which has appeared, and I hope will continue to appear, in our transactions, material helpful to the practitioner, for it is a record of the difficult and unusual cases, which the medical profession has referred to the Hospital.

The members of this Society realize that they must not stand aloof from the members of our great State Medical Society. Anything which will place us in closer touch with the medical profession of the State, will surely work to our mutual advantage, and this Society can be the means of making such bonds closer.

In closing, let me say that the future of this Society depends upon the individual efforts of each one of you. Nothing can be accomplished without hard work. It is oftentimes a hard and disagreeable task to attend a medical society meeting when one is mentally and physically exhausted by a long day's work. Yet we have chosen a profession where such days come all too frequently, but we must find time for the kind of work this Society stands for. else we fall to the level of those doing a vast amount of practical work with no written record of all that has been done and seen which would be helpful to others.

Therefore I bespeak your co-operation to make the coming year of this Society the most successful in its existence.

Reports of Cases

A CASE OF MULTIPLE INTRAUTERINE FRACTURES.

D. MURRAY COWIE, M.D.
CLINICAL PROFESSOR OF PEDIATRICS AND INTERNAL MEDICINE,
UNIVERSITY OF MICHIGAN.
(From the Pediatric Clinic, University Hospital, Ann Arbor, Michigan.)

The case I wish to report is as follows:

William D., age three weeks, entered the Pediatric Clinic of the University Hospital, August

Fig. 1. Photograph showing natural position of infant

14, 1913 because of a congenital deformity of legs, hands and feet.

FAMILY HISTORY—There have been no deformities on either side of the family. The mother is twenty-eight years old, the father twenty-nine. One brother is living, six years old, and healthy. The mother has had no miscarriages.

ANTE-PARTEM HISTORY—When four months pregnant the mother slipped and fell, striking the left side of abdomen. She feared she would

abort and remained in bed after the fall, although she had no abdominal pain. The mother is a large woman, weighing 185 pounds. One month later (5th month) she fell down two steps. She caught the railing and in so doing

Fig. 2. Showing fracture of right humerus

wrenched her side. She was frightened several times during her pregnancy.

BIRTH HISTORY—The labor was full term. Pains were first felt at 5 A.M. They did not become marked until 6 P.M. At 10 P.M. the pains became severe, and at 10:30 P.M. the child was born, no instruments being required. The infant was deformed at birth, as shown in the illustrations. Resuscitation had to be resorted to.

PAST HISTORY—The infant was unable to nurse the breast, but has gained in weight since it was put upon the bottle. Birth weight not known, present weight 5 pounds 8 ounces. The bowels have been constipated, requiring oil. There have been no gastric symptoms. The skin has always been clear and free from eruptions, as has also the mouth and anus.

PRESENT CONDITION—The patient prefers to lie on the right side with the head thrown back against the spine. The head is flexed with difficulty, circumference 14 inches (normal 14½ inches). The anterior fontanelle is very small, 2cm. in diameter. The head is fairly well shaped. Ears show no stigmata of degeneration. The left leg is drawn up and the right is partially extended. The left upper extremity is constantly held in the position shown in the photograph. (Fig. 1.) The right, while not under the patient's control, is found in different positions. Both feet are clubbed, the left more than the right. There is a marked thickening over the upper third of each femur, giving the appearance of a fracture. There is no crepitus and the masses are hard. There are marked dimples of the large joints, giving the appearance of scars. (See knee and thigh, Fig. 1.) The hands are perfectly flat, especially the left, which gives the appearance of a hand cut out of card-board. The thenar and hypothenar eminences are absent. The fingers of the left hand are somewhat spindle shaped and curve inward. The hand is broad, 3.5 cm. as compared with the right, 2.8 cm. The arms and left leg cannot be extended. There is a peculiar clear smooth redness of the skin of the right hand and fore-arm. The pupillary reflexes are normal. There is no nystagmus. The tendon reflexes cannot be elicited. The testicles are not felt in the scrotum. The prepuce is adherent. The skin and mucous membranes are negative. The nasopharnyx is shallow.

Examination of the lungs and heart is nega-

Fig. 3. Right humerus at another angle, showing repair

tive. The abdomen is difficult to examine because of the head being thrown backwards, making it tense. There is bulging in the flanks as shown in the photograph. This is soft and is due to the position.

RADIOGRAPHIC EXAMINATION shows a fracture of the left femur, right femur and right humerus. (Figs. 2 to 5) All of the fractures show advanced repair.

Examination of blood, urine and stool is negative.

True intrauterine fractures are rare. In a search through the literature Dr. Richard Smith succeeded in finding forty-three cases, these with his own case making a total of forty-four. In all of these cases a history of injury was obtained, the

most common being a fall or a blow on the abdomen. Less frequent causes in this series were bullet and gunshot wounds, and other piercing wounds of the abdomen. Five of the cases were multiple fractures.

In many of the recorded cases the lightness of the injury, apparently responsible for the fracture, is of great interest. It suggests some important predisposing cause. In some, the accident occurred before quickening. It seems hardly probable that a fall unless very severe would produce a fracture in utero at this time. It is well known, however, as we have had illustrated by a case in the children's clinic in a boy of nine years, that in *osteogenesis imperfecta* a fracture may occur spontaneously by the exertion of no greater force than that required to change the dressings, or through some sudden movement of the patient. In my case the first accident occurred before quickening, the second, of slighter degree, at about the time of quickening.

Of the three predisposing causes, osteogenesis imperfecta, rickets and lues, the former is probably the most important. From a study of the bone structure in this case I feel safe in making the statement that it belongs in this group. Some cases of intrauterine fracture have been mistaken for achondroplasia. The two conditions are entirely different, clinically and pathologically. Such a mistake could hardly be made in this case even without a radiograph for it is easy to see that the bones have grown in length, in other words, the cartilage is evidently proliferating normally. In osteogenesis imperfecta there is a faulty bone metabolism, the calcification is imperfect, and the disease is confined to the shaft of the bone.

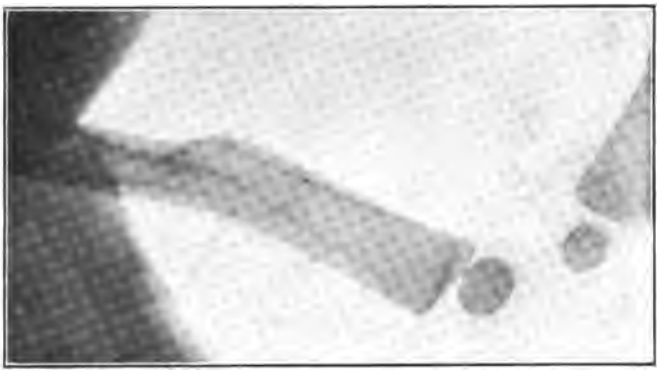

Fig. 4. Fracture of left femur

Fig. 5. Fracture of right femur

The cartilage is normal in shape and size. The bones are always brittle. Some authors believe there is such a thing as fetal rickets. There is a great difference of opinion upon this point. It it not at all improbable that many of the cases regarded as fetal rickets are cases of achondroplasia, a condition which is not so likely to predispose to fracture.

I am sorry Doctor Camp is not here to discuss the question of paralysis in this case. There is a paralysis of both upper extremities and it seems to be peripheral. I believe it may be accounted for by an injury affecting the nerve trunks. The paralysis is more marked on the right than on the left side. The early closure of the fontanel and the position of the head argues, however, in favor of central involvement.

DISCUSSION

Dr. Reuben Peterson: I have read carefully Dr. Smith's most interesting and valuable paper upon the subject under discussion. Probably in this case the injury to the mother had nothing to do with the fractures since the fall was about the fourth month of gestation However, fracture is possible even this early, as shown by Smith in one case. As a rule, the fetus is very well protected from external violence by the amniotic fluid and the abdominal walls which contract quickly under the influence of trauma. With flabby walled women, especially if the child be carried low, it would be possible for such fetal fractures to occur. It is well for practitioners to bear in mind the possibility of intrauterine fracture, so as to guard against a law-suit when the child is born with a deformity, since the X-ray would soon establish the correct diagnosis

Dr. Cyrenus G. Darling: I was particularly interested in one point in the case reported by Dr. Smith The intrauterine fracture had united but with a resulting deformity. On the twentieth day after birth the child was operated upon and the ends of the bones placed in position. Still, the X-ray showed a deformity and a second operation became necessary. The bones were reunited with chromicized catgut, and the patient made a good recovery. It is interesting to note how early in life these deformities may be corrected and good union take place. In the case just reported, the value of any operative procedure is very doubtful on account of the paralysis.

THREE CASES OF SECONDARY SYPHILIS

John H. Stokes, M.D.

Resident in the Department of Dermatology and Syphilology, University of Michigan.
(From the clinic of Dermatology and Syphilology, University Hospital, Ann Arbor, Mich.)

The three patients, whom I wish to show are all cases of lues, in the active secondary stage and all three still showing the primary lesions in various stages of involution.

Case I. This is the case of Mr. C., who entered the Hospital with a brilliant maculo-papular rash. A feature of special interest in this case is the way in which he acquired his infection. We are, of course, sufficiently accustomed to expect the venereal exposure as a source. This man admits exposures but they were, according to his statement, all prior to his marriage a year and a half ago. The source of his infection is extramarital, but it is also extragenital. The patient is a bartender, and in the course of his duties, he was obliged to eject a drunken patron from the saloon in which he was employed. The man made an active resistance and the patient found it necessary to strike him in the mouth. In so doing he cut the knuckle of the second finger of his right hand upon the man's upper teeth. The wound bled profusely at the time and was cleansed with peroxide by a druggist, who also applied a salve whose nature we do not know. For a week the patient had considerable pain from the cut, which, however, presently healed over and ceased to trouble him. About two weeks after the occurrence he first noticed a swelling at the site of the injury which enlarged slowly without affecting the mobility of the joint, and presented some bluish discoloration. The intumescence has remained essentially unchanged since reaching its present size, and the almost cartilaginous induration beneath the scar of the injury must be apparent to all of you. The lesion is a hard chancre. This man has developed an extramarital primary, which is of a sufficiently well-known type to have received a special name —the brawl or fist chancre. It may serve as a vivid reminder to us of the risk which each and every one here may take when he strikes a tough or other opponent on the mouth with the naked fist, whether in self defense or in assuming the aggressive in response to an affront. Incidentally, with the history of the use of an ointment before us, let me remind you of the prophylactic virtues of the calomel ointment in 40 per cent strength, when promptly and vigorously rubbed into an abrasion open to the suspicion of having become infected with pallida. The absence of superficial erosion or ulceration in this case does not, in the face of the circumscribed, non-inflammatory, painless induration, invalidate the diagnosis of hard chancre. The last link in the chain of evidence establishing the specific nature of this lesion was obtained by Dr. Wile's aspiration of a small amount of lymph from the deeper portion of the induration with an ordinary hypodermic syringe. In this lymph we had no difficulty in demonstrating the presence of three or four pallidae to the dark field, one-twelfth oil immersion. The generalization of the infection from its initial site was of course followed by the outbreak of secondaries, of which his brilliant rash is the most striking. The eruption is polymorphous in character and may be described as a maculo-papulo-squamous, or more briefly as a large papular syphilide.

A number of the lesions, especially on the trunk, were almost psoriasiform in type. The moment one glances at the eruption, however, one feels instinctively the indefinable premonition that this will on closer examination prove to be specific. The only rash with which this might reasonably be confused is that of a variola in the pre-pustular stage. The differentiation from the eruption, objectively, depends upon such factors as the distribution, the rash in this case involving the trunk too much for a variola, and the entire absence of any sign of actual or impending pustulation. The process moreover is an indolent one, the individual papules being of a much less lively tinge than the acutely inflammatory variola papules. The presence of the roseola with the papular rash is also an important element in the differentiation. If we permit ourselves to use the anamnesis, the entire absence of the characteristic prodromata of the variola eruption further establishes the specific nature of this rash. A very interesting feature brought out by this case is the inverse relation which exists between the large papular syphilide and the occurrence of mucous membrane lesions.

This patient, in spite of the extensive involvement of the skin, presents practically no involvement of the mucous membranes. In addition to the frank eruption this man presents other evidences by which we may estimate the severity of his infection. He has lost twenty-five pounds in weight in a few weeks, has marked nervous symptoms, has nocturnal osteocopic pains, cephalalgia, and according to his history, was for a time so prostrated as to be compelled to remain in bed. All these considerations identify the type of disease from which this man is suffering as the asthenic with the nervous symptoms perhaps somewhat more accentuated than usual. He has a marked general adenopathy, in connection with which let me call your attention to the striking difference between the epitrochlear of the right arm and that of the left. The axillary glands on the right are perhaps also somewhat larger than those on the left. This is, of course, somewhat more than the general secondary adenopathy —it is in fact the painless, indolent satellite bubo of this man's extragenital chancre. You notice that I wear gloves rather from habit than from necessity in this case. Contact with the rash so long as the patient's skin remains unbroken does not expose the examiner to the risk of infection, although of course the spirochaeta are present here beneath the unbroken cutis of the papules as they are in fact in every definitely syphilitic lesion. Should the surface of one of these papules, however, become eroded as it might, especially where moist surfaces are in contact, such a lesion would at once become a source of infection. This patient is married and it is, of course, a matter of importance to discover whether or not his wife and young child have been infected. Balancing the probabilities, in view of the absence of the highly contagious mucous membrane lesions the prospects seem good that they have escaped. We have, however, drawn blood from the mother for a Wassermann test. The patient's Wassermann is strongly positive.

Case II. The second case which I want to present is one that came originally to the Surgical Clinic. This is C. B. nine years old, who was brought to the Hospital on account of a trouble with his hip, which is apparent at first glance. He is one of a family of a considerable number of children, all of them older than himself. The mother is dead and the father died last June of what was reported to be an ulcerating tumor on the face. There is no history of miscarriage and the children, as far as lues hereditaria is concerned, are entirely free. The patient had been with his father within a week of his first entry into the Hospital, on May 14th. He was discharged from the Surgical Service June 26th, and from that time until he re-entered on September 15th, he was under the care of his grandmother. During his first stay in the Hospital, no evidences of any skin lesion are reported. When he was brought to the Hospital the second time, however, there was a large eroded and ulcerating area on the scrotum at the root of the penis. The grandmother, according to the boy's statement, had given the lesion local treatment and it had been seen by his home physician, who apparently had found no reason to suspect its real nature. On Sept. 17th, his secondary rash was noticed for the first time.

As regards the length of time that the boy had had the scrotal erosion we have only the boy's statement that he first noticed the chafing and irritation from his trousers on June 26th, the date of his previous discharge. This would place the time of his initial infection in all probability prior to his first entry into the Hospital, when he was living with his father. When his general condition first attracted attention he had a roseola covering his entire body with the exception of the head, neck, face and hands. The possibility of an exanthem led to an immediate consultation on his case and the patient was seen by Dr. Wile. While the rash was macular over the body there were several discrete papules on the penis and by abrading the surface of one of these Dr. Wile demonstrated the presence of the pallida by dark field examination. The case was a distinctly puzzling one, although on analysis only one area over the left hip could well have passed for an early measles even had the distribution been typical. The relation between the area on the scrotum and the secondary outburst quickly became ap-

parent. This, too, is a hard chancre, conforming in a general way to the primary lesion described by Fournier as *chancre hypertrophique* although, of course, the tremendous intumescence of the hypertrophic chancre of the face, as described by him, is not present here. The general induration is less apparent now perhaps than before treatment was begun but I think you can easily see the more localized infiltration at the base of the penis which represents the remains of the true chancrous induration. You note also the slightly eroded area over the surface of the indurated plaque. This entire area is then the boy's primary lesion—a giant chancre. Just previous to his first injection of salvarsan given on the 21st, he showed the slight temperature, characteristic of the secondary stage. Following his injection he reacted violently, the picture being that of the typical Herxheimer reaction and indicating that the boy was full of pallida. His temperature rose rapidly to 104° about six hours after he received the salvarsan and was entirely unaffected by the tepid sponge which was ordered for him. It fell to normal as promptly towards morning. His roseola was considerably more vivid on the morning following his treatment, illustrating, of course, the typical temporary lighting up of the infection characteristic of a Herxheimer. The second injection, given on the 27th, in which he received twice the initial dose of fifteen hundredths grams, resulted in no reaction. The boy is now rapidly improving, although I think those of you who are near enough can still see, in spite of the artificial light, the last traces of the roseola on the trunk, showing through the normal *marmor cutis.*

The prognosis, of course, is of great interest in this case. It may be tersely expressed as bad in young children and very old men. Dr. Wile considers this boy's prospects of a complete recovery as very good. Had the boy been in the hands of even fairly competent medical advice at home, it is quite conceivable that an error in diagnosis would have allowed him to develop some perhaps serious tertiary accident before he came under treatment. The origin of the boy's infection, I am sorry to say, we are not as yet able to establish. The boy states that one of his married sisters had a blotchy rash and that he used her towels. How much of this has been suggested, of course, is problematical. The site of the lesion at the base of the penis lends color to the suspicion that this boy has been subjected to indecent practices and that contact with somebody's mouth or somebody's vulva is responsible for this primary sore.

Case III. Mr. R. a case of secondary syphilis. The patient came to the Hospital with a sore mouth and a rash over the body. He gave a history of clandestine exposure, followed several weeks later by the development of a small, hard papule on the penis. The lesion did not reach a very large size and under treatment is now well on the road to involution. I think, however, you can all see the remains of the hard chancre on the prepuce and note the elevated, indurated plaque and the raw-ham coloration so often mentioned in Fournier's classic descriptions. The skin manifestations consisted simply of a roseola on the trunk and papulo-squamous lesions on the palms and soles. The patient, however, had a mouth full of mucous patches and a number of papules on the dorsum of the tongue. In this particular he illustrates, as did Mr. C., though in the opposite way, the inverse relation between the mucous membrane and skin manifestations in the secondary period. The patient is of the asthenic type, showing a marked loss of weight, fourteen pounds in nine weeks, a specific cephalalgia, arthralgia and myalgia, all of which showed the characteristic feature of syphilitic secondary pain—nocturnal exacerbations coming on especially after the patient is warm in bed. The arthralgia affected the left elbow and although the patient complained of slight stiffness, absolutely no evidence of joint involvement could be discovered.

This man's tibiae are especially interesting. Even at this distance I think you can note the non-inflammatory thickening due to a local periostitis upon the anterior surface of the bone in the right leg. Such a process, while not a true gummatous infiltration, is perhaps a rather advanced secondary manifestation. The highly localized excruciating tenderness on pressure is very characteristic of this form of periosteal involvement. The tenderness practically disappeared and the pain in the left elbow has cleared up following three injections of neo-salvarsan.

I might also call your attention to a rather rare condition which this man presented on entering—a secondary papule on the plica semilunaris at the inner canthus of the right eye. This is homologous in every way with a papular syphilide anywhere else on the body but its occurrence at this site is distinctly rare. I am sorry that arseno-therapy has deprived you of the pleasure of seeing it to full advantage. The papules on the tongue, those of you in front will have no difficulty in seeing. You note, of course, that they are elevated and that the surface shows no sign of the superficial erosion, with slight inflammatory areola and the grayish pellicle, characteristic of the mucous patch. We are, of course, interested again in estimating the virulence of this man's infection. He has a tremendous adenopathy, a finding not usually associated with a malignant syphilis. On the other hand even this early in the disease there is a marked involvement of the central

nervous system. Although the patient states that he has had no eye symptoms, ophthalmoscopic examination of his fundus shows that he has a neuro-retinitis. We should, therefore, be inclined to rate this as a rather severe case. Paradoxical though it may seem, this man is to be congratulated on the multiplicity and severity of his symptoms, which have brought him within reach of vigorous and systematic treatment. It is to be expected that under efficient management and with proper co-operation on his part, his infection will run a mild course to complete cure. Before I have him stand up for your inspection of his adenopathy I want to call your attention to the annular whitened areas on the soles of his feet which represent the scaling remains of his papulo-squamous syphilide. The fact that all asthenics do not conform in every particular to an absolutely uniform type is brought out by the fact that Mr. C., whom I first showed you, has a very large, easily palpable spleen, while this man's cannot be felt.

You notice the remarkable discrete painless adenopathy in the cervical region on this patient. He might almost pose as a model for the visible demonstration of the occipital and posterior auricular, the parotid, the submaxillary and the anterior and posterior cervical lymphatic ganglionic groups. There is an equally striking enlargement of the inguinal, epitrochlear, axillary and femoral nodes. This is also an exceptional opportunity for us to post ourselves on the location of the sub-mammary node, at the lower border of the pectoralis major muscle. You note that it lies like a buck shot under the skin. On entrance he presented another evidence, possibly of lymphatic involvement, in the form of a localized cylindrical swelling like a pipe stem under the skin on the inner aspect of the right calf. While it was hard and exquisitely tender, there was no sign of active inflammation, or of edema, discoloration or prominence of the superficial veins such as one would expect with a thrombophlebitis. The condition was interpreted as a lymphangitis, such as is sometimes seen on the penis during and after the presence of the primary lesion. The possibility of a periphlebitis was also thought of, and I must confess that with the light striking it as it does now, what remains of the linear infiltration is practically continuous with the visible elevation caused by the internal saphenous vein.

1608 Geddes Ave.

DISCUSSION

Dr. Harry B. Schmidt: I would like to ask Dr. Stokes if that lesion on the bone of the lower leg could be a tertiary lesion. Recently several internists have described secondary and tertiary lesions in the heart of patients in the secondary stages of syphilis. I recently saw a case, referred by Dr. Wile in the secondary stage of syphilis, who after salvarsan developed a bradycardia. The question arises whether the salvarsan produced this or a syphilitic heart disease.

Dr. D. Murray Cowie: This patient entered the Surgical Clinic for treatment of tuberculosis of the hip. He had been discharged and re-entered for further treatment. When he left the hospital there were no signs of scrotal involvement or eruption. Soon after re-entering, the scrotal lesion was observed. Its nature was not recognized until after the eruption developed. He was referred to the department of infectious diseases, Dr. Crissy being then in charge, who made a provisional diagnosis of lues and referred the case to Dr. Wile who confirmed the diagnosis.

Dr. Stokes (closing the discussion): The case that Dr. Schmidt has just mentioned was a very interesting one indeed. The young man was of the asthenic type. He was given a rather large initial dose of neo-salvarsan and had a marked reaction. At six o'clock the following morning his pulse and temperature were normal. He got up and walked down stairs without permission but later returned to bed. Within half an hour his temperature began to fall and his pulse fell with it. The drop continued until his temperature had reached 96.6° and his pulse 60. It was in the eighties on entrance. The boy looked yellow and had passed no urine for a considerable length of time. We were genuinely alarmed and immediately began vigorous stimulation. Under strychnine, local heat, hot coffee and whiskey enemata his condition improved during the day and the indefinable toxic expression and listless, drowsy manner passed off. During the night, however, his pulse fell to 46 and his temperature to 96°. On auscultation only a slight irregularity in rhythm was apparent. Several days later his treatment by neo-salvarsan was resumed and he received three other injections without complications.

The point which Dr. Schmidt brought out about the close relation between secondary and tertiary lesions I have heard frequently emphasized by Dr. Wile. The differentiation between a secondary and tertiary lesion in some usages of the term is based on chronology and refers to time rated from the initial lesion. It seems to me that the pathological basis for the distinction, which makes gummatous infiltration the essential characteristic of the tertiary period is a more rational one.

Relative to Dr. Cowie's point in connection with the boy, I might explain that Dr. Cowie was absent from the city at the time and through some inadvertance there was a miscarriage of the refer slips. We were not aware that the case had been diagnosed as secondary lues before it was seen by Dr. Wile

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TWO CASES OF CARCINOMA OF THE PROSTATE

Ira Dean Loree, M.D.

Clinical Professor of Genito-Urinary Diseases, University of Michigan.
(From the Genito-Urinary Clinic, University Hospital, Ann Arbor, Michigan.)

The two patients whom I wish to present for your consideration are males, fifty and fifty-seven years of age. They both came to the Hospital because of difficulty in passing urine. The elder man has been sick since July and the younger man about the same length

of time. They have both passed some blood, and while the elder is able to empty the bladder with a great deal of difficulty, the younger patient has almost complete retention. They have both had pain, not only across the lower abdomen but radiating to the thigh, perineum and glans-penis. On rectal palpation the elder man had a rather hard nodular mass in the region of the right lobe of the prostate, while the palpating finger in the other encountered a small mass of stony hardness not confined to either lobe.

On the above findings the clinical diagnosis in each case was carcinoma. In the elder man I performed a palliative operation, opening the bladder through a perineal incision for drainage and the relief of his pain and discomfort. At the same time a small portion of the tumor was removed for pathological examination, which, later, confirmed the clinical findings.

The younger man who, because of his retention most needed the palliative operation, desired to return home for a time before undergoing operative interference.

Carcinoma of the prostate may be divided into two classes, namely, intra- and extra-capsular. A large number of the former class that have come under my observation have shown an area of beginning malignancy in a lobe where senile hypertrophy had existed for a much longer period of time. The existence of malignancy is not suspected until the microscopical examination has been made and a large majority recover after an enucleation of the gland.

In dealing with the extra-capsular variety the surgeon sees but few cases that are favorable for the Young operation, which consists of total extirpation of the gland with its capsule, a portion of the bladder wall and the seminal vesicles. I have one patient operated four years ago by this method with a very gratifying result, the history of which I have already reported. In a large proportion of these cases as I have already stated, the only aid we can render is palliation for the relief of a distended bladder or the pressure of the neoplasm upon the nerves.

ADDISON'S DISEASE WITHOUT PIGMENTATION. REPORT OF A CASE WITH AUTOPSY

HARRY B. SCHMIDT, M.D.

Instructor in Clinical Microscopy, University of Michigan. (From the Medical Clinic, University Hospital, Ann Arbor, Michigan.)

The patient, Mr. P. K., laborer, age 32, entered the University Hospital, August 20, 1913. As the patient was a Greek and unable to speak English, the history is rather uncertain. All that could be obtained was that he had been sick in Detroit before he came to the Hospital. He complained of severe headache and diarrhea, because of which he had to quit work and was confined to his room for four days. He was then taken to the Marine Hospital, where he stayed eighteen days and was then dismissed as well. While in the Marine Hospital he had a very severe epistaxis. For a time after his dismissal from the hospital he felt fairly well but complained of being extremely weak and had several fainting spells. Since August 17, he has become much worse, has had very severe headaches, does not remember of having had chills, complains of feeling very hot and having pain in the splenic area and to the right of the umbilicus. He is greatly constipated. He does not remember having seen any blood in his stools.

The patient looks very sick and is apparently slightly chilly. His pulse is small, quick and frequent, but not dicrotic. His tongue and mouth are clean, his throat not reddened. The thorax moves well; breath sounds are clear and the heart sounds approach tic tac rhythm. The patient rests with his knees drawn up. The abdomen is rigid and below the level of the ribs there is no distention. The spleen is firm and easily palpable, and there is considerable gurgling in the abdomen. No generalized or local tenderness can be made out, although the patient points to the abdomen with motions of distress. Rose spots were looked for on several occasions but never found.

On August 24, a Widal in 1-10 dilution was positive in twenty minutes. Widal in 1-50, no clumping in one hour. On the 25th., the Widal in dilution of 1-30 clumped in twenty minutes.

The temperature at the time the patient entered the hospital ran between 100.4° - 102° with pulse between 96 and 102. Respirations were 24-28. The patient had seven stools on the first day of entrance, afterwards the bowels were moved by enema. For four days after entering he ran a continuous irregular temperature up to 102.8°. On the 5th day his temperature fell to normal and on the 4th of September his temperature became subnormal, ranging between 96° and 99° by rectum. His pulse after the temperature fell ran between 78 and 88. His temperature remained subnormal until the day before he died, when it arose to 102.6° by rectum. During this time his mental condition was apathetic at all times, but occasionally he had hallucinations of sight with mild delirium. For two weeks his pulse was of very low tension, very small and at times was imperceptible at the wrist. His heart sounds were very faint and approached tic tac rhythm. Most of the time, the sight of food seemed distressing to him and for two weeks

before his death he refused almost all nourishment taking only an occasional spoonful of milk or albumin water. The urine examination was negative. Blood examination showed 5,290,000 red cells, 7,100 whites and hemoglobin of 90%. Stools were negative. The systolic blood pressure taken on the 14th of September was 65.

An early diagnosis of typhoid fever was made because of the positive Widal in dilution of 1-30 in twenty minutes and he was treated as a frank case of typhoid fever with a post-typhoidal psychosis up to the day he died. No blood cultures were taken. However, in view of the low blood pressure, retracted abdomen with peculiar onset, and prolonged subnormal temperature, a final diagnosis of miliary tuberculosis with involvement of the adrenal glands was made before the autopsy, in spite of the fact that no pigmentation of skin or mucous membranes could be found.

The autopsy disclosed caseous tuberculosis of the mediastinal lymph nodes, extensive pleural adhesions, small heart with brown atrophy and fatty degeneration. There was enlargement and hyperplasia of the spleen, hyperemia and enlargement of Peyer's patches, enlargement of the retroperitoneal glands and mesenteric lymph nodes and caseous tuberculosis of both adrenals. No disseminated tubercles were seen in the liver, spleen or kidneys nor in other parts of the body. Examination of the brain was negative.

It has often been noted that Addison's disease without pigmentation usually runs a rapid course, as was the case with our patient. The enlargement of the spleen is rather uncommon in this condition.

In conclusion: A patient sick in the Hospital for thirty days and indisposed for some time before this was believed to have typhoid fever. On account of a prolonged subnormal temperature and low blood pressure together with other atypical manifestations the diagnosis was ultimately changed to Addison's disease without pigmentation and this diagnosis was confirmed at autopsy.

DISCUSSION

Dr. James H. Agnew: I saw this patient early in his febrile period. A Widal in dilution of 1-10 was positive, and 1-50 negative. Later on another Widal was taken and a dilution of 1-30 gave a positive reaction. As far as the Widal is concerned it is the custom in this laboratory to take as a standard a dilution of 1-50, which if positive should clump in one hour. We also generally take a 1-10 dilution, as a check for any gross error. In this case while a positive reaction in 1-30 dilution should not have been considered, yet every so often in early typhoid, we find these beginning reactions.

I did not see the patient after that, but upon my return, was told he died of Addison's disease. The most significant feature of this was the absence of pigmentation, which may not be extensive but is practically always present at some stage of the disease. We often find other signs and symptoms in Addison's lacking but the pigmentation can generally be depended upon.

As regards the diagnosis of miliary tuberculosis, I would say that the physical signs in the chest were negative. No X-ray was taken because the physical examination did not indicate it.

VOLUME V.

TRANSACTIONS OF THE CLINICAL SOCIETY OF THE UNIVERSITY OF MICHIGAN

STATED MEETING, NOVEMBER 5, 1913

THE PRESIDENT, R. BISHOP CANFIELD, M.D., IN THE CHAIR
REPORTED BY REUBEN PETERSON, M.D., SECRETARY

Reading of Papers

STUDIES ON THE ETIOLOGY AND TREATMENT OF GONORRHEA.

CARL C. WARDEN, M.D. (Michigan '95)
LOS ANGELES, CALIFORNIA.

The diagnosis of gonorrhea has been in part based on the microscopic appearances of stained smears made from the purulent discharge. Probably in a majority of cases this procedure is adequate in the early stage of the disease, since the microscopic picture is then characteristic and invariable, but as has been stated by Schwartz, McNeill and others, the diagnosis of chronic gonorrhea depends upon cultural methods aided by the complement fixation test. As these authors have stated, the positive gonococcus complement fixation test means the presence of a focus of gonococcus somewhere in the body. Late in the course of the disease the test becomes negative and gonococci cease to appear in cultures, yet it is common experience to observe intracellular cocci in the exudate. The question arises whether the usual microscopic examination of smears is a safe criterion of the presence of gonococci. In a recent article[1] I endeavored to show that many, if not all, the intracellular, biscuit shaped and Gram negative cocci which make up the diagnostic picture may not be gonococci at all, but are organisms of the species staphylococcus, and I based this conclusion in part on the following observations:

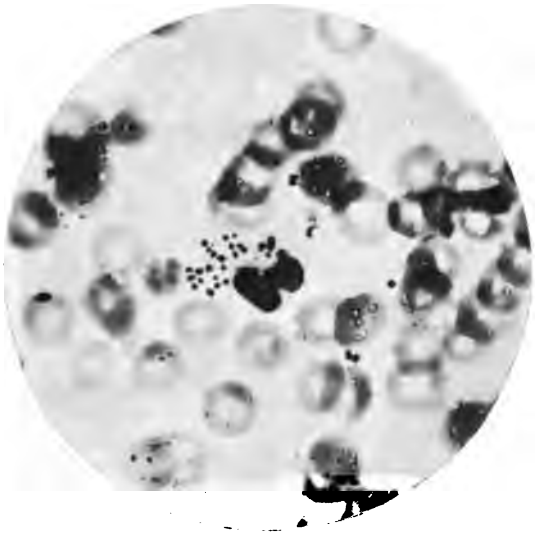

Fig. 1

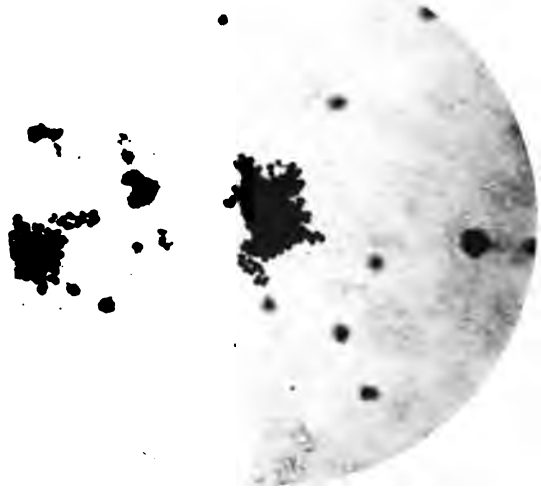

Fig. 2

1. The normal urethra is the habitat of a staphylococcus albus, to which I have given provisionally the name of staphylococcus urethrae which is capable of taking on virulence (infestiousness) under certain conditions just as the coccus of Welch in the skin and the staphylococcus in the throat.

1. Journal of the Infectious Diseases, July, 1913.

Dried, dead, sterile gonococci, gonococcus autolysate and sterile tryptic ferments when placed within the healthy urethra cause transient discharge in which intracellular biscuit shaped cocci are demonstrable.

2. The staphylococcus urethrae is invariably present in cultures from gonorrheal urethritis. Pure, or almost pure cultures of gonococcus are exceedingly rare, and as I have stated elsewhere, appear to have special significance of impending epididymitis.

Fig. 3

3. The staphylococcus, ordinarily positive to the Gram stain, may lose the stain in the presence of serum and leucocytes. The diagnostic picture of gonorrheal pus smears may be reproduced artificially, in vitro, with staphylococcus, whereas it has been impossible to do so with gonococcus.

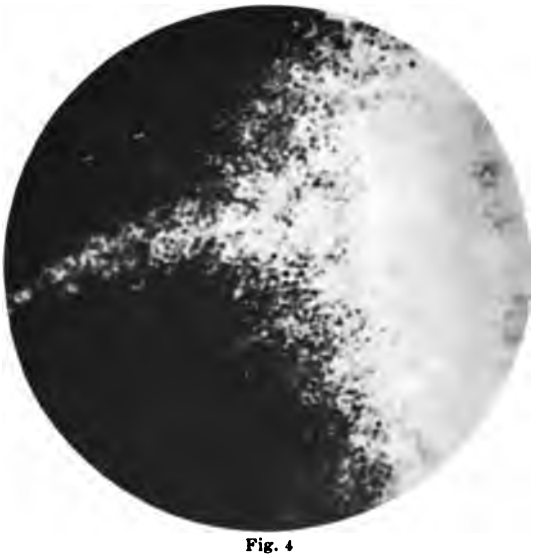

Fig. 4

4. By special methods of cultivation it is possible to observe the growth and multiplication of the intracellular cocci, and their development into colonies. In the same cultures the development of the gonococci may be studied and the differences in characters of the two organisms noted.

5. The staphylococcus in the presence of human serum or ascites in hydrocele fluid normally develops as a biscuit shaped diplococcus, and in this form is capable of losing the Gram stain. On ordinary media the diplococcal form is rarely seen, the individuals being spherical, clumped and positive to the Gram stain.

Fig. 5

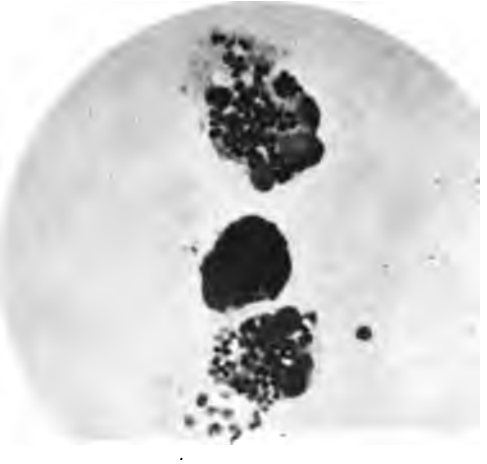

Fig. 6

6. The gonococcus upon the same body-fluid media is distinguished by its irregularity in size, morphology and staining. The biscuit form is not characteristic. It stains feebly with methylene blue, even with heat, and the individuals seldom show clear-cut outlines, many being shadowy. Autolysis is one of the

most prominent characters and is to be observed in the youngest colonies.

7. There is little or no affinity between the virulent gonococcus and the leucocyte. The gonococcus ferment, like the leucoprotease of the pus cell, is tryptic in character, and the latter especially is fatal to the growth of the organism.

8. The gonococcus does not produce true abscess in animals or man, that is, it is not a pus producing organism. The products of disintegration (autolysates) are toxic and will cause sterile exudates. The staphylococcus, on the other hand, is a pus producing organism.

These observations and others have led me to infer that the staphylococcus which has been regarded largely as a concomitant and accidental organism may be assigned a definite place in the etiology of gonorrhea. A casual relation to the disease we may believe would scarcely assure the formation of antibodies in the serum of the gonorrheic patient, whereas the serum of such patient possesses at certain periods some degree of staphylococcus lysins, immune opsonins, and produces deviation of complement. There is never at any time during the course of an uncomplicated case of gonorrhea very considerable antibody formation either to staphylococcus or gonococcus, else the symptoms of illness would be more pronounced. Antibody and antigen affect slight combination so long as the latter is remotely confined to the urethra, but once bacteria reach the epididymis or the joints, symptoms of constitutional reaction appear.

A further inference assigns the staphylococcus and gonococcus to a symbiotic relationship in the disease. Just what factor is responsible for the heightened infectiousness of the staphylococcus is not altogether clear. Evidently the ferment of the gonococcus is not alone this cause. The simplest explanation appears to lie in the life and growth of the gonococcus, and the stimulus is manifest throughout the diesase and apparently persists often long after gonococci have disappeared from cultures and complement fixation has ceased.

How extensive a rôle the gonococcus plays in epididymitis and arthritis is problematic. My own cultural experiments lead me to believe that here the staphylococcus has an important part. A striking symptom of epididymitis is the cessation of the urethral discharge. I have been able to produce a like diminution by inoculations of dead staphylococci, but not with gonococci. At all events the symptom is due to autoinoculation.

If the staphylococcus occupies the place assigned to it the next inference would be that any treatment not directed against it, as well as against the gonococcus, must be erroneous. Gonococcus antisera have proved disappointing. Gonococcus vaccines appear to serve little purpose. When fresh they may be toxic, and when old they are quite inert. It is my belief that it is possible to develop a method of treatment along immunologic lines which will meet the exigencies of the double infection. Such a method aims to supply the body of the infected individual with the antibodies which it appears to be unable to manufacture in large amount for itself, by means of an immune serum, and at the same time to create in the patient's system an active immunity by introducing antigen, or in other words by inoculating with staphylococcus suspensions. By this means, a combination of active and passive immunization, it is expected to assist the body in speedily overcoming an infection which is so localized and remote from the factory of immunizing substances that ordinarily the response is very slow. This expectation has been fulfilled sufficiently in practice to warrant further effort. I am at the present time working on such biologic products and shall soon be prepared for a more extended trial of them.

DISCUSSION.

Dr. Udo J. Wile: The paper of the evening is certainly instructive to all of us. I am certain that many cases of gonorrhea are overtaxed as the result of finding intracellular organisms which are thought to be gonococci but are, according to Dr. Warden, unquestionably staphylococci. The demonstration of the staphylococcus invariably in gonorrhea suggests that there may be a symbiosis and one wonders whether or not the staphylococcus may not be responsible for the purulent character of the disease. Weight is given to this possibility by the fact that gonorrheic conjunctivitis is always purulent. The staphylococcus is a normal habitant of the conjunctiva, whereas we assume the gonococci alone to be responsible for gonorrheic arthritis, in which case the exudation is not purulent. In connection with epididymitis it has been suggested that the cessation of the discharge from the urethra is due to the high temperature, it being a fact that the gonococcus cannot survive long at a high temperature.

The close similarity of the meningococci and gonococci has been made use of by Heitz-Boyer of Paris, who uses very successfully a vaccine of meningococcus in the treatment of gonorrheic arthritis, epididymitis, and orchitis.

Dr. Frederick R. Waldron: There seems no question but that Dr. Warden has proved that our morphologic diagnosis of gonorrhea is not conclusive and that the typical intracellular Gram-negative diplococci are not gonococci. I do not think he has emphasized enough the work I have seen him do in his laboratory. He takes cultures from a case of gonorrhea and shows in his ascitic fluid slide cultures we have always taken to be typical gonococci, intracellular Gram-negative diplococci, developing step by step into large colonies from which he takes subcultures. These pure cultures retain their original characteristics while grown on special media at body temperature and can be put abundantly into leucocytes where they make a typical picture of gonorrhea. But this same culture will grow on ordinary culture media, lose its Gram-

negativism and revert to the typical round staphylococcus form and vice versa. The real gonococcus he shows to be an organism behaving in a radically different way.

I am convinced that we must be rather careful about making a final morphologic diagnosis of gonorrhea. However, I am not convinced that typical clinical gonorrhea, smears from which show the generally accepted picture, cannot be safely treated as such, whether it is a case of symbiosis or reversion.

The great importance of Dr. Warden's work, aside from its pure scientific value and its suggestions as to Gram-negativism, seems to be its possibilities, so far as the making of vaccines and immune sera is concerned. Anyone who has used these agents in the treatment of chronic gonorrhea and its complications cannot fail to be impressed with what they accomplish in a certain percentage of cases. Many cures in from twenty-four to seventy-two hours of cases of very acute gonorrheal rheumatism of the most typical kind can be ascribed to no other agent than the vaccine. Serum treatment, also, is often followed by an immediate disappearance of the organisms from the discharge in many chronic cases. Yet the many absolute failures with both agents leave much to be desired. This may be entirely changed by Dr. Warden's work.

Whether the brilliant results were due to gonococcal or to a peculiar staphylococcal vaccine cannot be known as he has often found that commercial gonococcal vaccine was being derived from a Gram-negative staphylococcal culture. That there is abundant clinical evidence of a symbiosis of a mixed infection, is supplied by the mixed vaccines furnished by the drug houses for years.

I cannot agree with Dr. Wile in regard to the reason for the often observed cessation of the discharge during an epididymitis and sometimes the apparent permanent cure of the disease. Concurrent fever due to something else might do the same thing, but this I have never observed. It is much more probable that the improvement and not infrequent cure is due to an autoinoculation.

In fact there are many things of just this kind that point to vaccine and serum therapy as being our great hope in the cure of this stubborn and dangerous disease. The character of the work demonstrated to us this evening gives us every reason to expect that Dr. Warden will be able to carry it to its logical conclusion.

Dr. D. M. Cowie: A point which Dr. Warden has not emphasized is the beautiful method he uses for the study and differentiation of the gonococcus colonies. With the materials at hand it is almost as easy to do this as it is to make the ordinary smear preparations. I have had the pleasure of going over this work with Dr. Warden and have been convinced of the practicability of the method in clinical work. The films of ascetic agar are spread on sterile slides; they are then put in a large Petri dish and placed in an incubator. From five to ten slides are easily accommodated in the Petri dish. A small dish of sterile water is placed in the dish to supply moisture. The next morning the slides are examined under the microscope with the one third objective. There is absolutely no difficulty in differentiating the very characteristic gonococcus colonies from the staphylococcus colonies. I believe this method could be made use of in the study of other micro-organisms of clinical importance.

Dr. James G. Cumming: Dr. Warden's work is not only interesting but very important inasmuch as it throws light on the evolution which the gonorrheal organism may pass through. I think any of us who have grown the organism on artificial media have noted the variation in its characteristics with the Gram stain. Dr. Warden's explanation of this and his demonstration by the slide method is original and of great value.

Dr. Warden (closing): I have done considerable work on epididymitis cases, and it hardly seems possible that the elevation of temperature could of itself cause the cessation of the discharge. A like cessation follows inoculations with staphylococcus, which procedure scarcely ever produces fever. By my method of culture one may observe the marked diminution of staphylococcus colonies both in cases of epididymitis and in those inoculated artificially, while the gonococcus colonies persist for some time.

The gonococcus is not a pus producing organism. My experience has been the reverse from those who claim that gonococcus only is to be obtained from the joints in gonorrheal rheumatism. I have never succeeded in growing the gonococcus but have invariably cultivated the staphylococcus.

The meningococcus strongly resembles the gonococcus. It is noteworthy that staphylococcus occurs in the cerebrospinal fluid in about 30 per cent. of diplococcus meningitis cases.

The question of relationship between the gonococcus and the staphylococcus is puzzling to me. While I have inclined to the idea of symbiosis, nevertheless I am unable wholly to get away from the possibility of direct biologic relationship through variation.

DESCRIPTION OF ILLUSTRATIONS

Fig. 1. Proliferation, on ascites agar, of artificially phagocyted staphylococcus urethrae, one hour after inplantation. X 1200.

Fig 2. The same, young colony at 6 hours. The leucocyte has been overgrown. X 1200.

Fig 3. The same, young staphylococcus colony 18 hours old. Shows the normal morphology of the organism on serum medium. Gram negative. X 1200.

Fig. 4. Margin of gonococcus colony 24 hours old.

Fig. 5. Smear from artificial urethritis, gonococcus excluded.

Fig. 6. Gram negative, intracellular, biscuit-shaped cocci, identical with smears in gonorrhea, produced artficially with staphylococcus urethrae.

Reports of Cases

A CASE OF TRANSCORTICAL MOTOR APHASIA.

Albert M. Barrett, M.D.

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(From the Psychiatric Clinic, University Hospital, Ann Arbor, Michigan.)

I desire to present a patient with an aphasic disorder of speech which suggests the type of the transcortical motor aphasia. The case is that of a woman, who is a patient in the Psychopathic Hospital and is now sixty years old. Her mother had been childish in her old age. The account of her own life given by her relatives developed nothing of importance, except that her school training was limited, as she did not get beyond the third reader. She, however, had learned to read and write and was described by her sister as a "brilliant and witty young woman."

About two and a half years ago she had

an apoplectiform attack. For a short time she was motionless, then began to talk and "spoke as plainly as she does now." She showed no paralysis and a few days later returned to her work. She performed her household duties acceptably until the spring of 1913, when her work was badly done and her memory much impaired. At times she was abnormally irritable. There were expressions suggesting delusions, such as "Blood had run out of her side." "At nights she had seen her dead parents." In this condition she came to the Hospital.

Physically she showed the appearance of early senility. The heart was not pathologic, and the blood pressure was 110. The blood and cerebrospinal fluid showed no pathology. The right hand grasp was a little less than the left and there was difficulty in the tests for muscle coordination. The important disturbance for our purpose here, was in the field of language. A summary of a large amount of material obtained from many examinations gives the following information:

She always understood the purposes of the examination and gave good attention until fatigued. She often became agitated at her inability to do things as she should and sometimes cried. There was usually a long delay before giving the desired reaction. She was right handed and showed good preservation of tone appreciation.

Reaction to words heard: Simple commands were always understood. When several commands were given in succession she correctly understood the first and often the second but rarely any more. Her attitude in these instances seemed to indicate that she could not remember what was asked. She correctly composed a number of words of from three to five letters when spelled to her. There was no paraphasia or perseveration in her verbal responses, but frequently, when fatigued or when several requests had been given in succession she found it difficult to free herself from a previous action.

Picking out objects when named: This was correctly done when the objects were at all familiar.

Reaction to things heard: She correctly recognized a number of objects from their characteristic sounds.

Repeating words and sentences from dictation: All words and simple sentences were correctly repeated without paraphasia. Longer sentences were often repeated in fragments as if she could not remember all that had been given.

Spontaneous speech: On the ward she spoke but little. She would answer questions and occasionally would volunteer a limited conversation. Usually when addressed on the visits of physicians she would answer without hesitancy questions regarding her health but there would be no further response until another question was put. Sometimes she could repeat the alphabet correctly but usually she would stop before she finished and then could not pick it up again at the place she had stopped. When prompted she would usually go on correctly. Sometimes numerals were intermingled among the letters. Counting showed the same difficulty. She spelled a few simple words of from three to five letters correctly but in the majority of instances a few letters were correct and others were wrong. Usually the number of letters in a word were correct and the incorrect letters given had some resemblance to those desired as: tree was spelled "troo". Michigan was started "Mig".

Reaction to things seen: It could not be demonstrated that there was any hemianopsia. Any exact determination by the perimeter was out of the question and the disturbances in her speech made even the reactions to rough tests unsatisfactory. Whatever tests were made did not suggest hemianopsia. She was presbyopic but there was no marked decrease in her visual acuity. She correctly named most familiar objects when shown to her. Pictures of many complicated structures such as machines she did not name. Scenes containing a number of figures in action were poorly described.

Reaction to words seen: The letters of the alphabet and numerals were usually correctly identified. A few simple words of from three to five letters were very rarely correctly given. Her name she usually picked out correctly. She was totally unable to read sentences, headings in newspapers or printed or written requests.

Reaction to things smelled: Wintergreen was called perfume but was not named more specifically. Further tests gave no correct reactions.

Reaction to things tasted: Salt was correctly identified. Vinegar was called sour.

Reaction to things felt: From both right and left hands she correctly identified the forms of a few geometric figures and correctly named a number of familiar objects.

Writing: She was totally unable to write. She usually began the test as if she would be able but the characters made had little resemblance to those desired. Copying was only possible in a few instances when she traced a few forms by following close to the lines of the figure.

Mimic and gestures: In no instances did she correctly react to motions indicating desired actions.

The internal language: It seems probable that in large part the internal language was preserved. The fact that she spelled many

words correctly and that, in her attempts at writing, the number of characters had a near relation to the number of the proper word would indicate this. The tests of Onuf and Liepmann were unsatisfactory owing to the apraxic disorder.

Apraxia: In most of her motor reactions there was a delay between the reception of the request and the execution. In repeating words and naming objcts the response was fairly quick. In executing commands there was a marked delay as if puzzled how it was to be done. A good example of this was the reaction when asked to point to her nose with her right hand. She looked at her right hand, moved her arm about, placed her hand on her knees and kept it there. When the command was repeated she put up her hand hesitatingly slowly approaching her nose and then grasped it as if pinching it. Asked to put her left hand on her forehead she put out both hands, looked at them in a puzzled way as if trying to decide which was the left, after having correctly decided she held it up and looked at the examiner as if not knowing what to do with it. When the command was repeated she placed the hand on her head.

She understood the use of objects such as a comb, glass, knife and fork and pencil. There was always much difficulty in their use but never were they used incorrectly. She was shown a comb and asked what it was used for. She replied promptly "to comb the hair." When asked to use it she took the comb in her hand, turned it about, fingering it in various ways, hesitatingly reached it up towards her hair and finally used it correctly.

The results of the examinations show that there is present an almost complete alexia, a total agraphia, diminished spontaneous speech, preserved repeating from dictation and a marked difficulty in the correct starting of many purposeful actions.

There is no disturbance on the receptive side of auditory speech nor on the emissive side and the path between the auditory and the motor speech regions is preserved. There is no perseveration. There is evidently some intelligence defect present. This is seen in the general dullness of the woman, her lack of interest in her personal care and a certain amount of emotional deterioration.

Clinically this group of symptoms resembles some of the descriptions of the transcortical motor aphasia, although the amount of voluntary speech that is preserved is more than in most of the cases described and the loss of reading and writing is more than usual.

The motor difficulty is of the nature of an apraxic disorder. The movement idea is always correctly formed and the auditory command is always understood. The difficulty is in the connections between the area where the auditory speech memories are deposited and the area where the movement idea is formed. It corresponds in this respect to Liepmann's ideokinetic apraxia.

To localize the disturbance is not altogether easy. The general intelligence disturbance and the marked memory impairment suggest a wide spread brain involvement and this is the process which has sometimes been found in the transcortical speech difficulties. The ataxia and agraphia are so marked as to almost make certain the localization of a disturbance in the region of the left angular gyrus. To account for the apraxia the lesion would have to involve the connecting fibers of the left auditory and the motor areas. Further than this it seems impossible to go at this time.

DISCUSSION.

Dr. Carl D. Camp: Dr. Barrett's case is interesting to me but the ground has been covered so fully from a neurologic point of view that I have nothing to add. It is only proper to remark that all of the cases on record show such great variations that for purposes of localization it is difficult to make use of these symptoms in any positive clinical way. It is naturally more or less of a guess what the lesion in each case is or where it is located.

BILATERAL INTERMITTENT SWELLINGS OF THE PAROTID GLANDS DUE TO INFECTION OF STENO'S DUCTS (SIALODOCHITIS).

Albion Walter Hewlett, M.D.
Professor of Internal Medicine, University of Michigan.
(From the Clinic of Internal Medicine, University Hospital, Ann Arbor, Michigan.)

Mrs. M. G., age thirty, came to the Medical Service at the University Hospital on May 5, 1913, complaining of swellings on the sides of her face. The family history was unimportant. In the past she had had some stomach trouble with belching and heart-burn, some menstrual irregularity and for the past eight years a leucorrheal discharge.

The present illness began in January, 1911. While tasting food in the kitchen she experienced a pain in the left side of her face, which was followed by an acute swelling in the region of the left parotid gland. This swelling, which was tender on pressure and which interfered with opening the mouth, lasted about two and a half hours and then disappeared spontaneously, leaving the side of her face somewhat tender. For the following three months these swellings recurred almost daily on the left side but since then both sides of the face have been affected. They come especially in the morning immediately after taking the first bite of food. During one of the attacks, the patient received a blow over the

swelling which caused it to disappear. The attacks have varied greatly in frequency but she has rarely passed a week or more without trouble and in the last nine months the swellings on one side or the other have been almost continuous. She has frequently been unable to eat on account of the pain. Her general health has become impaired and her weight has fallen from 128 to 101½ pounds.

The examination showed a poorly nourished young woman, quite pale and with bilateral tender swellings of the parotid glands, which prevented her from opening her mouth freely. Examination of the insides of the cheeks showed that the papillae upon which Steno's ducts emptied were considerably swollen, reddened and quite hard to the touch. Mucopurulent material could be obtained from the mouths of the ducts. Probing failed to discover any calculus or other foreign body and an X-ray of the cheek was negative. Upon several occasions it could be shown that pressure upon the parotid gland caused considerable fluid to come from the duct and that while the first few drops were mucopurulent, that which followed was clear mucus. Microscopic examination of the mucopurulent material showed numerous pus cells but no organisms.

It was therefore evident that we were dealing with a bilateral inflammation of the terminal portions of Steno's ducts, the symptoms of parotid swelling being due to obstruction of the excretory ducts by a swelling of the mucosa or by a plug of mucopurulent material. It is interesting that the early attacks occurred only on taking food, which naturally excited the gland to vigorous secretion. The tendency of attacks to occur after the first food taken in the day, is also interesting, because it seems probable that during the night the absence of salivary secretion allowed the ducts to be more effectively obstructed by the mucopus. The disappearance of the swellings on one occasion after a blow upon the side of the face, may also be interpreted as being due to a dislodgement of the mucous plug in the duct.

The treatment consisted first in daily instillations of a 10 per cent. argyrol solution into the ducts and second of frequent massage of the glands, so as to keep the ducts open Under this treatment the condition rapidly improved. The trouble which had been practically continuous for eight or nine months became better, the parotid swellings disappeared, and the material obtained from the ducts lost its mucopurulent character. The general health of the patient also improved; the hemoglobin rose from 45 to 84 per cent. and the lost weight was recovered.

An operation for curettage of the uterus and repair of perineal lacerations was performed in Dr. Peterson's department on May 18.

The patient has reported a number of times at the Hospital for examination since her discharge on May 31. She states that she has had occasional slight attacks of parotid swelling with pain in this region but she has had no severe attacks since leaving the Hospital. Examination of the ducts on the occasions of her return have always shown an absence of acute inflammation. The swelling and redness of the papillae have not returned and the parotid secretion has remained clear.

DISCUSSION.

Dr. D. M. Cowie: A very interesting disease for which this condition may sometimes be mistaken is that known as Mikulicz disease. This condition is characterized by painless bilateral enlargement of the parotid, sublingual, and orbital glands. It occurs in children as well as in adults. Some twelve or thirteen cases have been recorded in children. It is not associated with the symptoms of acute inflammation. There is a well known type of intermittent inflammatory parotitis. Dr. Hewlett's case is of interest from the viewpoint of retention resulting from apparent stenosis of the ducts and evidently does not resemble this latter type.

A CASE OF CHYLURIA.

Harry B. Schmidt, M.D.

Instructor in Clinical Microscopy, University of Michigan. (From the Clinic of Internal Medicine, University Hospital, Ann Arbor, Michigan.)

Mr. F. J., age fifty, American, married, entered the University Hospital on October 6, 1913, complaining of painful urination, constant dull pain in the bladder region, following which he passes milky urine.

History—His family history is unimportant. He has had the usual diseases of childhood, but never scarlet fever nor typhoid. He had pneumonia at 35 and gonorrhea at the same age. At the age of 42 he had sciatica. He denies having had syphilis. There was never any tuberculosis in the family and the patient has never been exposed to tuberculosis that he is aware of.

About a year ago the patient first noticed that his urine occasionally resembled milk. At this time for four or five weeks he complained of a dull pain in the bladder region with some difficulty in passing the urine in the morning. During the past year he has had fifteen or twenty similar attacks, coming on irregularly and at times apparently brought on by excessive exercise. The last attack began October 1, 1913. The urine at this time was slightly cloudy and on the following morning he had pain in the bladder region and passed a much cloudier urine than the previous night. This urine had the same milky color. The patient thinks that this attack may have been precipitated by splitting wood the day before.

The dull pain in the bladder region still exists but is not as bad as formerly. He has never had any chills, fever nor sweating in any of the attacks and the urine has never contained blood. The amount of urine passed during the attack is much smaller than normal and he has often observed clots which resemble milk curds. Occasionally they cause some difficulty in micturition. As these attacks usually begin after arising in the morning, he

thinks that posture may play an important part in their causation.

The patient seldom coughs, and has never had any night sweats nor fever in the afternoon. He complains of some slight shortness of breath on exertion, but has never had any edema of the extremities or of the genitals. His appetite is fair, and his bowels usually are regular. He has never been jaundiced nor had clay colored stools. He has lost about forty pounds, and has not regained this since the first attack. The patient's home is in Michigan, and he has never been out of the state except for seven months which he spent in Colorado and two visits to the state of California.

Physical Examination — Physical examination showed a well nourished muscular man of good color. There is no general glandular enlargement. The heart and lungs are negative. The edge of the liver is distinctly palpable but apparently not enlarged. The spleen is not palpable. There is no enlargement on percussion, and no elephantiasis. The genitals are normal. On examination, the eye grounds show arteriovenous compression, and there are myopic changes.

The Von Pirquet tuberculin test after forty-eight hours gives a slight reaction to 25 per cent., but is otherwise negative. Three milligrams of tuberculin given subcutaneously after thirty-six hours give a marked local reaction with no general nor focal reaction. The Wassermann is negative. Cystoscopic examination of the bladder is negative and the phthalein test from the catheterized ureters showed that the left kidney is excreting normally. No fluid was obtained from the right kidney because of kinking of the catheter on that side.

At the time the patient entered the Hospital his urine was negative. The patient was placed in bed and given an excess of fats without results. A few days before he left the Hospital, he had an attack of "milky urination." The specific gravity of this urine was 1009. It was negative to the Fehling's test. It would not clear on boiling nor upon the addition of acids. Microscopically the urine contained very small refractile granules. There were neither casts nor ova and no parasites seen in the sediment. The test for albumin was positive. Shaken up with twice its volume of ether, it lost its milky color, the resultant fluid being of a turbid grayish appearance.

On October 15, 1913, the urine was again perfectly clear and negative upon examination. His blood was examined carefully; on two occasions at night, about 10:00 P.M. and 1:00 A.M. No filaria were discovered. There were 5,000,000 red cells and 7,800 whites and a hemoglobin of 85 per cent. (Meischer) The systolic blood pressure was 125. Examination of the stools was negative. The temperature remained normal during the time the patient was in the Hospital.

Diagnosis—Since no definite etiologic factor could be found in this case, the diagnosis of idiopathic chyluria was made.

These idiopathic chylurias are relatively rare. It has been observed that they run an intermittent course, as do the chylurias of filarial disease. They are more or less noticeably affected by posture, many cases exhibiting a tendency to show chyle in the urine after arising in the morning. In thirty cases reported in the literature, in two instances a pelvic or inguinal abscess preceded the chyluria. Magnus Levy reported a case of chyluria with milky urine from the right ureter at night or only when the patient lay in the recumbent position. Dr. Saxton Pope has reported a case of chyluria in a Japanese school boy who had had Pott's disease and psoas abscess in infancy. As shown by a cystoscopic examination, the chyle came from a sinus which opened in the region of the trigone. Ludke has reported a case of chyluria with inflammation of the bladder. Several cases have been reported, especially that of Charteris where the disease has been markedly influenced by posture and Hertz reports a case with obstruction above the diaphragm.

In conclusion, the chylurias due to filarial disease and also those of idiopathic origin, are conceded to be due to a rupture of the lymphatics, either of the bladder, kidneys or ureter. Very few of the nonparasitic chylurias have come to autopsy. Up to 1908 only four have come to autopsy in Germany. Of these but one, that of Hertz, was due to obstruction. It would seem, however, that in all probability in all of these cases there is an obstruction to the lymphatics in the bladder, kidneys or ureter. However, it is impossible to demonstrate this obstruction at autopsy or clinically in the majority of cases.

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DISCUSSION.

DR. JAMES H. AGNEW: This patient came complaining of some painful and difficult urination during these attacks. This was probably due to the small plugs or agglutinations of fatty material which form in the bladder in this condition. He had no symptoms whatever during his attack in the Hospital and neither were any of these plugs passed. One of the striking features of the urine was the perfect emulsification of the fat. A specimen after standing for a week or more showed no tendency towards the formation of a fat layer nor could the fat be separated by centrifuging.

DR. D. M. COWIE: It would be interesting to know the per cent. of fat in this patient's urine. This can be easily determined by the Babcock method which I have used a number of times, in the examination of chylous fluids. I believe we had a case of chyluria in the Medical Clinic a few years ago in a Chinaman. The man came to the clinic and was examined. His urine was found to be opalescent. He did not remain long enough, however, for complete examination and we were unable to follow up the case.

DR. CHARLES B. G. DE NANCREDE: I have seen at least two cases of chyluric ascites in the absence of all evidences of filariasis. On one I made an abdominal exploration which resulted in an apparent cure, but a chyluric pleuritis succeeded the abdominal condition. About forty years ago I saw a similar chyle-like fluid which had been removed by a colleague from the tunica vaginalis testis. Unless my memory deceives me, Doctor F. P. Henry reported a case of chyluria occuring in Philadelphia where

the filaria were detected in the blood, although the patient had not resided in any locality where filariasis had ever been reported.

Dr. A. W. Hewlett: The filarial type of chyluria is due to an obstruction of the lymphatic passages by the adult filarial worm. This causes a dilatation of the lymphatic channels with ruptures into the urinary passages. The mechanism which causes the non-filarial type of chyluria is not well understood. Of the few cases that have come to autopsy some have shown no definite disease of the lymphatic system, and in others the cause of the chyluria was not evident.

Dr. Schmidt (Closing): The patient brought this specimen to the Hospital. It was passed on October 1 this year and has stood in the laboratory ever since. You see that it is perfect emulsion, also that it has not separated into layers.

A CASE OF MOLLUSCUM CONTAGIOSUM OF THE EYELIDS.

Dennis V. Smith, A.B., M.D.

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The patient, M. H., female, aged eight, came to the clinic about six weeks ago complaining of redness and swelling of the left eye. Ever since an attack of the measles her eyes had been red and weak, but four weeks previous to her coming to the Hospital, the condition became very much aggravated and small growths appeared along the lid borders.

History—The family and personal history were negative as regards the eye condition. The patient was well developed and with the exception of enlarged adenoids and tonsils was quite healthy.

Examination—Examination showed the vision to be 5/7.5 in both eyes. Pupillary reflexes were normal. In the right eye there was slight conjunctival injection, and in the slightly thickened upper lid there was a small nodule one millimeter from the lid order and five millimeters from the inner canthus. The skin over the nodule was slightly tense and glistening but was fairly movable. In the left eye both lids were thickened with narrowing of the palpebral aperture and slight mucopurulent discharge at the inner canthus. The palpebral conjunctiva was distinctly hyperemic with small discrete papular elevations causing a roughened and thickened appearance. The ocular conjunctiva was injected. The iris and cornea were apparently normal.

Along the roots of the cilia of the upper lid and external to the intermarginal line were two small nodules, one about three and the other about ten millimeters from the inner canthus. These were about one and one-half millimeters in diameter at the apex and about one millimeter high. The base was slightly broader and reddened, while the apex was finely granular, yellowish white and slightly umbilicated. About the middle of the lower lid border there was another nodule less elevated and broader than the two above.

Diagnosis—A diagnosis of molluscum contagiosum was made and confirmed by the Department of Dermatology.

Treatment—Upon incising the apices of the growths the contents were readily expressed as a finely granular whitish substance resembling sebum. The lesions were then treated with silver nitrate and soon healed over, leaving a slightly indurated area at the site of the growth.

While the case was under observation two small indurated areas appeared on the cornea, one at the limbus at 4, and the other one millimeter inside the limbus at 8. The larger one at 4 had a ring like border with central yellowish infiltration and a clearer zone between. Several other small whitish vesicles appeared near the limbus but they all responded readily to calomel and a pad, leaving a fine superficial vascularization of the cornea.

DISCUSSION.

Dr. Udo J. Wile: Molluscum contagiosum is more frequently seen in the skin than in the eye clinic, although the lesions do occur on the lid margin, being carried there undoubtedly by the fingers of the patient. The etiology of the disease is as yet unknown but it is highly probable that there is a filtrable virus. In an epidemic of molluscum contagiosum I endeavored unsuccessfully to inoculate my own skin with material expressed from a lesion and it seems not unlikely that infection occurs only where conditions are suitable in those perhaps predisposed. It is interesting to note that pigeons have a condition closely allied to molluscum contagiosum. A small epidemic of this disease occurred in Ann Arbor last year. I saw some six or eight cases at that time.

TRANSACTIONS
OF THE
CLINICAL SOCIETY
OF THE
UNIVERSITY OF MICHIGAN

STATED MEETING, DECEMBER 3, 1913

THE PRESIDENT, R. BISHOP CANFIELD, M.D., IN THE CHAIR
REPORTED BY REUBEN PETERSON, M.D., SECRETARY

Reading of Papers

FAMILY SUSCEPTIBILITY TO CANCER

ALDRED SCOTT WARTHIN, Ph.D., M.D.
(Professor of Pathology and Director of the Pathological Laboratories in the University of Michigan, Ann Arbor.)

It has long been recognized that a family susceptibility to certain forms of benign neoplasms exists. Many of the peculiar "family marks" or "birthmarks" distinguishing the members of certain family lines are neoplasms usually of a mature connective-tissue variety, chiefly hemangiomas, lmyphangiomas or fibromas (moles, warts, nevi, "strawberry mark," "raspberry mark," etc.). Lipomas, chondromas, osteomas, neurofibromas, gliomas, leiomyofibromas, papillomas, adeomas and cyst-adenomas have been observed to "run" in certain families, and most authorities agree as to the existence of a family susceptibility in the case of these neoplasms. Certain varieties of carcinoma and sarcoma are also regarded by various writers as showing a less marked family tendency.

As to a general susceptibility to cancer appearing as a definite family characteristic, authorities at the present time are divided. Its existence is denied by some, and as strongly affirmed by others, but as a matter of fact there are very few good statistical studies of the family occurrence of carcinoma. Cancer surveys have yielded little of value because of the great difficulty in obtaining immediate knowledge of members of a given family for more than one or two generations. It is a well known fact that few hospital patients can give any definite information as to the cause of death of their grandparents, and the same thing is true of the population at large. It is only in rare instances that a complete family history extending over several generations can be obtained. Further, when such rare complete family histories covering a number of generations can be obtained, it must be borne in mind that the diagnosis of cancer a generation or two ago was almost wholly a clinical one, unsupported by microscopic examination; and that the common clinical diagnosis of "tumor" covers a very large and heterogeneous class of conditions, the majority bearing no relationship to carcinoma. It is obvious that such a diagnosis has no statistical value; but, as a matter of fact, many of our so-called "cancer statistics" are based upon just such loose clinical statements. This is, however, no argument for rejecting all of the diagnoses of cancer that have been made without the corroboration of the microscopic examination. Particularly in the case of lip, stomach, breast and uterine cancers may clinical diagnoses or family traditions be relied upon with a high degree of certainty. The outward appearances of breast and lip cancers, the striking symptoms of gastric and uterine cancers, in connection with a malignant course and fatal termination offer very fairly reliable criteria for both a clinical diagnosis and family tradition of cancer of these organs; and the percentage of error is probably not very great in so far as these conditions are concerned. In the case of other diagnoses of "abdominal cancer" or "tumor," "cancer of the liver," etc., the precise nature of the affection is very doubtful.

Throughout the literature, particularly that relating to cancer of the breast, there are recorded instances of the multiple family occurrences of cancer. Few of these consider more than the members of the same or of two generations, and usually the affected members alone are taken into account. Such statistics give little information beyond the fact of the multiple occurrence of cancer in certain family groups or generations. Of recorded observations of the multiple occurrence of cancer in one family for several generations the one of Broca (Traité des Tumeurs, 1866, p. 151) is the most important. In brief, this family showed cancer in sixteen out of thirty-seven

members, as follows: Madame Z, died at the age of sixty of cancer of the breast. She left four daughters (A, B, C, D) who died of cancer of the liver (2) and cancer of the breast (2) at the ages of 62, 43, 51 and 54 respectively. Madame A had three unmarried daughters, alive and well at ages of 68, 72 and 78 years. Madame B had five daughters and two sons. First son died, without issue, at 54, of cancer of the stomach. First daughter died at 35 of cancer of breast; second at 35-45 of cancer of breast; third, at same age, of cancer of breast; fourth, at same age, of cancer of liver; while the fifth died at 60, non-cancerous. All of the children of Madame B were without issue. Madame C had five daughters and two sons. The first son died in the army without issue; the second son was alive and well at the age of 72. He had one son dying at 18, and one daughter alive and well at 24. The first daughter of Madame C died at 37 of cancer of the breast, leaving two sons and three daughters. The first of these was alive and well at 58, having three healthy sons; a second son died young without issue; first daughter died in child-bed at 28; second daughter died at 49 of cancer of the breast, bearing two healthy daughters; the third daughter died of consumption at 41. Madame C's second daughter died at 40 of cancer of the breast, leaving one healthy son; her third daughter died unmarried, at 47, of cancer of the uterus; the fourth daughter died, at 55, of cancer of the breast, leaving two sons alive and healthy; while her fifth daughter died unmarried at 61, of cancer of the liver. Madame D had an only son alive and well at the age of 70.

Williams (Natural History of Cancer, 1908) has collected from the literature many examples of the multiple occurrence of cancer in families and family groups, and also added valuable observations of his own. In 370 female cancer patients he found a history of heredity in 83 or 22.4 per cent.; in 136 cases of mammary cancer there was a family history in 24.2 per cent., and in 142 cases of uterine cancer a history of heredity in 19.7 per cent. Such percentages, as Williams points out, are very high from whatever point of view they may be regarded. Butlin finds a family history of cancer in 37 per cent. of cases of mammary cancer. Nunn estimates such a family history in breast cancer as 29.3 per cent., and Lemp at 23 per cent., all of these estimates agreeing fairly closely. In certain families, as in Broca's case, the cancer chances are greatly increased, fifteen to twenty times that of individuals of the general population. If the chances of cancer for the individuals of certain families are fifteen to twenty times greater than for the individual of the general population, we must concede the existence of a family tendency to cancer, since such high percentages of occurrence in certain family lines cannot be explained on the grounds of environment, infection, or mere coincidence. Particularly is an assumption of a family tendency justified when the cancer affects the same organ or tissue of one sex through a number of generations, as in the case of Warren, the patient, patient's father, grandfather and great-grandfather all dying of cancer of the penis; and another instance reported by Earle of a patient with epithelioma of the scrotum, whose brother, father and grandfather all died of the same condition.

Williams from his own experience and collected cases, therefore, regards the statistical evidence in favor of family susceptibility to cancer as very strong. He states that inherited cancer manifests itself much more frequently in the female, although as often derived from the paternal as from the maternal side of the house. In cases of multiple family cancer there is an especial tendency for the females to be affected. He notes also the atavistic and collateral inheritance of the susceptibility to cancer, and the frequent association of tuberculosis, arthritic manifestations, and excessive fecundity. He believes that the majority of cancer patients are the *surviving members of tuberculous families;* hence advances the proposition that no inheritable condition is more favorable to the development of cancer than that which gives proclivity to cancer. Nevertheless he abstains from interpreting his collected facts in Mendelian terms, although he believes that the time will soon come when it will be advantageous to study the whole question from a Mendelian standpoint. He regards the great prophylactic question to be: "How in breeding to render a dominant tendency to cancer recessive."

Levin (*Zeitschrift für Krebsforschung,* 1912) is the first to make a eugenical study of the influence of heredity on cancer from the Mendelian standpoint. With the assistance of the Eugenic Record office at Cold Spring Harbor, Long Island, he has collected data from five families, two being fairly complete, the other three as yet fragmentary. These families are studied from the broad standpoint of the entire family line for six generations, and then by family groups in which one or more members suffer from cancer. The analysis of the family line as a whole shows that the incidence of cancer is not greater numerically than that of the general population. One thing is brought out in this study that does, however, speak for an influence of heredity upon cancer, and that is the occurrence in certain generations of cancer groups with a cancerous ancestor on either paternal or maternal side, or on both. The percentage of cancerous members in each cancerous fraternity corresponds closely to the

Mendelian percentage of members with recessive unit-characters in a hybrid generation, running in the eight cancerous fraternities analyzed from 10-33 per cent. of cancerous members to non-cancerous (Mendelian ratio 25 per cent.). Levin concludes that resistance to cancer is therefore a dominant unit-character, the absence of which creates a susceptibility to cancer. He also notes that the family susceptibility is specific for certain organs, in one family the uterus, in another the breast are the organs particularly involved. This had already been shown by Williams, who also emphasized the fact that in the males of the affected family the gastro-intestinal tract is usually the seat of the cancer, while in the female members the breast or uterus is affected.

A great increase of interest has recently been awakened in the subject of heredity in cancer by numerous observations upon the occurrence of cancer in certain strains of white mice and rats. It has been noted by a number of workers in this line that a greater proportion of spontaneous cancers occurred in mice purchased from certain dealers. While this fact was at first used as an argument for the infective nature of mouse cancer it was shown later that in the case of a strain of mice showing a high percentage of spontaneous cancers a much greater proportion of successful transplantations of the cancer could be obtained than in the case of strains showing few or no spontaneous tumors. According to Leo Loeb the incidence of successful transplantations in some strains showing a high occurrence of spontaneous cancer is practically 100 per cent. In Well's laboratory, breeding experiments with such susceptible strains of mice are being carried out on a large scale, and the facts so far observed speak for the existence of an inherited cancer susceptibility. Although denied by Bashford the occurrence of such a familial tendency to carcinoma in mice is generally accepted at the present time, because of the following observed facts: *Certain strains of mice do not develop spontaneous carcinoma, and such strains are resistant to transplantation of carcinomas from other mice; on the other hand, other family strains of mice show a high frequency of spontaneous carcinoma, and such strains give a high percentage of "takes" to transplantations.* Tyzzer has carried out breeding experiments with such strains but was unable to find that such a cancer susceptibility was transmitted according to Mendelian principles. Levin and Sittenfield (Proceedings of the New York Pathological Society, Oct., 1910) concluded from their investigations of the influence of heredity in cancer of the white rat that *resistance to the growth of an inoculable cancer in this animal behaves in the manner of a Mendelian dominant unit-character.* The observations of the part played by heredity in mouse and rat cancer are still too limited for us to draw any final conclusions; but, with the breeding experiments now being carried on, on a large scale by a number of workers, the problem may soon be settled.

In the *"Archives of Internal Medicine," November, 1913,* I have published the results of a statistical investigation of the cases of carcinoma examined in my laboratory during the years 1895-1913, for the purpose of determining what influence heredity might have had in the etiology of these cases. During these years there were 3,600 cases of neoplasm examined in the Pathological Laboratory of the University for the purpose of diagnosis. Of these 3,600 neoplasms 1,600 were carcinomas; and it is with these 1,600 cases that the present investigation was concerned. The great majority, about 90 per cent., of the material came from the state of Michigan; and as the University Hospital is not a charity hospital, it represents very well the average population of the state. The usual difficulty of obtaining a complete family history of hospital patients exists here also, although a teaching hospital and with much greater care taken in this direction than would be carried out in the average city hospital. About 30 per cent. gave full histories with details of several generations; and it is in these detailed histories that evidence of a family tendency to cancer stands out. I have for several years been getting the impression that a family susceptibility to cancer was very striking in some families, and that in such families there was a tendency for the neoplasm to appear at an earlier age in the youngest generation, and to run a more malignant course. Whenever, then, we have had a case of carcinoma in a relatively young individual I have made an especial effort to obtain the family history. As a result our records show an increase in recent years of histories showing a multiple occurrence of cancer.

From the records of the carcinoma cases I have selected the most striking of the cases of multiple family occurrence of cancer. Four families stand out prominently because of the striking proclivity to cancer shown in three generations. Charts illustrating these families are given in the *"Archives of Internal Medicine,"* but the abstract of the family histories is reproduced here.

Family G.—In this family a fairly complete survey was made of the two generations derived from a cancerous grandfather with a traditionary history of cancer in his life and a grandmother with a normal family history. From these there were ten children, five males and five females. Two of the daughters died of cancer of the uterus at 55 and 40 years, while two sons died at 42 of cancer of the stomach, and a third one at 45 of cancer of the abdomen.

All five of these individuals were married to normal partners without a family history of cancer, and all had issue, as follows: Oldest daughter who died at 55 of cancer of the uterus, had ten children; one daughter operated on at 42 for "cancer" of the uterus and still living; another daughter operated on at 22 for uterine tumor and bilateral dermoids of ovary, and still living. The remaining eight children are all living and well, only two being over 40 years of age. The second daughter, who died at 40 of cancer of the uterus, had four children, two sons and two daughters, all dying of cancer, the two sons of cancer of the stomach and intestine, and the two daughters of carcinoma of the uterus. The third daughter, living and well at the age of 75, has three normal children living at the ages of 47, 50 and 55. Four children had no living issue. The eighth child, a son, died at 42 of cancer of the stomach. His wife was of normal family history. They had eight children, of whom two daughters have died of cancer of the uterus at 40 and 44 years, while the remaining six are all living and well below the age of 40. The ninth child, a son, died of cancer of the stomach when between 40 and 42 years of age. He left six children from a marriage contracted with a woman of non-cancerous family history. One daughter died at 42 of cancer of the uterus, three children died of tuberculosis between the ages of 18 and 25 years, while two others are living and well at the ages of 32 and 29 years. The tenth son died at 45 of cancer of the abdomen, most probably primary in the stomach. He left, from a marriage contracted with a woman of non-cancerous family, seven children, of whom one died at 42 of cancer of the stomach and liver, another at 47 of cancer of the intestine, while a third was operated on at 42 for tumor ("cancer") of the uterus and still lives in apparent good health. Four others are living and normal at the ages of 45, 35, 30 and thirty.

Of the forty-eight descendants of the cancerous grandfather seventeen have died or been operated on for "cancer." The preponderance of carcinoma of the uterus (ten cases) and of the stomach (seven cases) is very striking in the family history.

Family F.—In this family the paternal grandmother died of "tumor." Her non-cancerous brother had two children, both of whom died of "cancer." Her only son died at 61 of dropsy. He married a woman who had two brothers who died of cancer of the stomach. She herself died of Bright's disease at 75. Her mother died of heart disease. The three daughters of this pair who show a double family history of susceptibility to cancer all had neoplasms; the oldest was operated on for tumor ("cancer") of the uterus and is still living; the second was operated on at 51 for myosarcoma of uterus, while the third daughter died of cystic tumor of the ovary. In this family history the preponderance of stomach and uterine neoplasms is also shown.

Family P.—The paternal grandfather had a nephew who died of cancer of the lip. In the first filial generation there was one daughter who died at 35 of cancer of the lip and a son who died at 86 of cancer of the scalp and cervical lymph-nodes. This son married a non-cancerous woman whose only sister had died at 47 of cancer of the rectum. From this union thirteen children, ten of whom (five brothers and five sisters) all died of pulmonary tuberculosis before the age of 30, while three remaining daughters had carcinoma of the breast, two dying at the ages of 36 and 42, and one operated on at thirty-five.

Family S.—The paternal great-grandfather died at about 70 of cancer of the stomach. His only son died at about 60 of cancer of the stomach, having married a woman who died at about 50 of cancer of the breast. They had six children, all of whom died of cancer; two daughters died at 80 and 60 of cancer of the breast, and another at 60 of multiple carcinoma of the breast, bladder and rectum. Two sons died of cancer of the stomach at the ages of 75 and 40, the third son dying of cancer of some internal organ, most probably the stomach. Only one son had issue, by marriage with a normal line. The only child died at 36 of cancer of the uterus. Of the eight descendants of the cancerous great-grandfather all died of cancer. As in Family P., the occurrence of carcinoma in both paternal and maternal lines apparently strengthens the susceptibility, both families becoming extinct.

A larger number of cases showing a family history of multiple occurrence of cancer through two or three generations are to be found in our records. Twenty-nine of these were selected as representative. Since the family histories are more or less incompletely given I have classed these histories under the head of "cancerous fraternities" or "cancer-generations." In general the normal members of the second and third generations are given, so that the proportion of cancerous to non-cancerous in two generations at least is exact. It was notable that the great majority of the cancerous fraternities occurred in small families; and in many of these the patient from whom the material examined for diagnosis came was the surviving member of the family line. In families showing these cancer-generations the carcinoma may appear in three or four generations, or there may be an intervening generation the members of which are not cancerous or more rarely a collateral transmission may be shown. In some cases all of the members of the small family are cancerous. By far the great major-

ity of these are females; and the family is in a large proportion of cases brought to an end by death of its female members through carcinoma of the breast or of the uterus.

The results of our study of this material may be summed up as follows: In the histories of the cancer cases coming from the state of Michigan and examined at the Pathological Laboratory of the University about 15 per cent. show a striking history of multiple family occurrence. When the difficulty of obtaining good histories is considered this proportion is relatively high; and, on the whole, corresponds fairly closely with the percentages obtained by Williams. We must conclude, then, that a definite and marked susceptibility to carcinoma exists in certain families and family generations. This family tendency is usually most pronounced when there is a history of cancer in both paternal and maternal lines. In such families there is an especial tendency for carcinoma to appear at an earlier age than in the forebears, and in these younger individuals the cancer usually shows an increased malignancy, developing more rapidly and setting up general metastases more quickly than in cases from which we can obtain no family history. Whenever we have a case of carcinoma appearing in an individual before the age of 35 we take especial pains to look up the family history with this especial point in mind to determine if there has been a history of cancer in previous generations; and in a relatively large number of cases this has proved to be the case. I therefore consider the prognosis bad in those cases of carcinoma in relatively young people who have a family history of multiple occurrence of cancer. This is also true in the cases of carcinoma coming from families where there is a history of tuberculosis on both sides. Our results corroborate those of Williams. We find that tuberculosis is the most commonly associated family disease in families having a multiple occurrence of carcinoma and that in many cases cancer terminates a family line that has suffered severely from tuberculosis. The association of the two diseases in families showing our cancerous fraternities is very striking. We also find, as did Williams, that many of these families a few generations back showed a high grade of fertility with large families of children, but that in the present generation there is a markedly lessened fertility and in many cases the cancerous individual terminates the family line. Family susceptibility to carcinoma we find to be shown in carcinoma of the breast and uterus in females and of the mouth, lip, stomach and intestines in the males. Rodent ulcer affecting some portion of the face shows frequently a history of multiple family occurrence in several generations. In the more complete family records studied the carcinoma manifests itself in the breast or uterus in the female usually, and in the gastro-intestinal tract in the male. This specificity of location has been noted by Williams, Levin and others. Next to tuberculosis we have found cardiac and renal disease most frequently associated with a family history of carcinoma.

Giving due consideration to possible errors in diagnosis in previous generations and the difficulty of obtaining accurate histories, I am still convinced that there is a definite and well marked family susceptibility to cancer in many family lines; and I think it is very probable that if we can have better and more complete histories the multiple occurrence of cancer in family lines would be found to be very much more frequent than our histories now show. I think we are perfectly safe in concluding that certain families show a definite cancer susceptibility and that this is inherited often in a progressive rate of inheritance, the susceptibility being dominant rather than recessive, as Levin concludes from his study. I do not think that the data are at present sufficient for us to apply the Mendelian principles to cancer heredity. Some of my cases agree fairly well with Levin's, the percentage of cancerous members in each cancerous fraternity corresponding fairly closely to the Mendelian percentage of members with recessive unit characters in a hybrid generation. If I considered the data sufficiently conclusive for any generalization, I would say that they point toward the existence of a progressive generative inheritance, the running out or extinction of a family line through the gradual development of inferior stock from an inheritance of susceptibility to tuberculosis and cancer, such an extinction often developing in two generations in a family previously marked for excessive fertility and longevity.

With the growing interest in eugenics and in family records very careful attention should be paid to all of these points, and in hospitals such as the University of Michigan Hospital, where such a large amount of cancer material is seen, a special effort should be made to collect accurate data concerning the families of cancerous patients. When such data are obtainable definite conclusions may be drawn.

Discussion.

Dr. Charles B. G. deNancrede: This paper is of great interest. The method employed by Dr. Warthin is to be commended, provided we bear in mind the fact that we never can correctly estimate the natural history of carcinoma or the unquestionable results of treatment until we understand the cause of cancer. Again, we cannot be certain of our pathologic data until two or more generations of competent pathologists have examined every specimen adequately, included in the statistics, because too many museum specimens now exist, which can yet be correctly diagnosed, which would be found incorrectly labelled if studied by a modern pathologist.

Dr. Warthin, when studying the eighteen hundred cases which have passed beneath his scrutiny during the past eighteen years, excludes two-thirds because the histories are inadequate, taking about six hundred, where the data seems fairly reliable. Of these, however, only about fifteen per cent. apparently demonstrate his views as to heredity. Of the cases with acceptable histories the majority were treated by me and in my service at the University Hospital. I regret to state that I am confident that many of the histories of my cases in the accepted class were decidedly unreliable and that of the remaining eighteen hundred thoroughly reliable accounts, if securable, might either enormously reinforce Dr. Warthin's arguments, or equally likely weaken his contentions. I have so often found my students' histories so misleading for even a clinical diagnosis, that when reliable evidence as to family history is requisite, I have to sift all the evidence myself, often being able to arrive at no conclusion or perhaps one absolutely different from that arrived at by the historian. I have a very distinct opinion regarding the lack of proof as to the hereditary nature of carcinoma, despite my early teaching that this was an unquestionable fact. Many of our convictions cannot be proved by actual evidence in our present state of inadequate information. If the experience of forty odd years have radically changed my opinion on this point there must be reliable grounds for such a change of front, which should have some weight.

I am also inclined to give some weight to the possible failure to eliminate from our historical, and their therapeutic statistics, the fatalities resulting from operations and their complications; were these always deaths from carcinoma, or were they assumed to be because of the fatal results, without adequate histologic examinations? Again, if these patients had not died as the result of operation, might not some of them really proved to have been cures, so vitiating the mortality results? These, and other objections must in all honesty be carefully weighed when attempting to decide any question merely or chiefly by statistics. The rather curious association of tuberculosis and carcinoma, which in my professional youth was denied as a possibility, has been verified in a number of patients, the specimens of which have been reported upon by Dr. Warthin.

I have been greatly impressed by the data presented by Dr. Warthin and hold myself ready to review anew my conclusions concerning the whole subject of carcinoma.

I trust that I shall not be understood as arriving at my conclusions concerning carcinomatous heredity from the six hundred cases included in Dr. Warthin's expurgated statistics, or the probable one thousand cases where I have been the operator or have in some way been cognizant of the patients, but what I learned in my hospital and private experience of the more than twenty years before I came to Ann Arbor.

Dr. Cyrenus G. Darling: While listening to Dr. Warthin's very able address, two points came to my mind. He says that the German cancer survey was without benefit, but he has not stated that a properly conducted survey might not be useful. Why not have such a Michigan cancer survey? Why should not such an important project originate in this Society? We know little or nothing about the results of our numerous operations for this disease, except in a few cases in our own immediate neighborhood. A survey might enable us to determine some of the important facts. It would be well for Dr. Warthin to prepare a list of questions which should be answered by every cancer patient coming to the University Hospital. This paper should be left with the house physician and made out by him as a part of the admission history.

Dr. Udo J. Wile: I have been amazed at the relatively large number of cases of cancer of the skin that occur in this vicinity. In a clinic in New York in which over three thousand cases were treated each year I can recall but three or four cases of epithelioma. During the past year at the University Hospital of over eight hundred cases treated there were forty-four cases of cancer of the skin. We have been careful to note in these cases the occurrence of any family history. Offhand I should say that about 15 per cent. give a history of cancers in other members of the family. Curiously enough these have been for the most part cancers of the skin also, rather than visceral neoplasms. We have also noted that the occurrence of cancer in the patient's family has usually been on the maternal side. I should be glad to turn over these records to Dr. Warthin should he desire them.

THE OCCASIONAL PRESENCE OF THE APPENDIX VERMIFORMIS ON THE LEFT SIDE OF THE ABDOMEN, WITHOUT TRANSPOSITION OF THE VISCERA EXPLAINED. ILLUSTRATED BY AN OPERATED CASE.

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(From the Surgical Clinic, University Hospital, Ann Arbor, Michigan.)

A brief preliminary summary of the facts pertaining to the development of that portion of the intestinal tract with which we are now concerned will obviate later explanations, will probably explain certain errors made when reporting cases, and, it is to be hoped, will prevent unnecessary manipulations and some disastrous errors when operating in the abdominal cavity. Only approximate estimations of the time after impregnation when the changes described are to be noted can be given, because they continuously progress, are not sharply defined, one observer considering as recently accomplished that which another considers in process of evolution.

About the close of the tenth week of gestation the somewhat left sided practically straight intestinal tube has assumed an U-form and the cecal bud and the rudiments of the appendix are recognizable, and the cecum occupies approximately the umbilical region. About the close of the fourth month the cecum reaches its usual prenatal position beneath the right lobe of the liver by a process of so-called rotation, passing in front of and across the superior mesenteric artery and duodenum, subsequently to descend into the right iliac fossa, this descent occurring, according to some observers about the sixth month of intrauterine life; according to others this may not occur normally until after birth.

While the few photographs[1] presented by no

1. George S. Huntington, Anatomy of the Human Peritoneum and Abdominal Cavity, page 60.

means exhaust the possible abnormalities of location and course of the colon, they should prove adequate for the present purposes. Numerous still more complicated and puzzling possibilities can obtain[2], induced by the traction of inflammatory adhesions alone, or from the effect of these, superadded to congenital variations; with such we cannot at present concern ourselves.

The patient, Paul B., age five, was admitted to the University Hospital October 29, 1913, having been ill eleven days. On October 18, he complained of headache, but so far as could be gathered nothing else was noted. The next day he said that he had severe pain in the abdomen, locating it chiefly on the left side. After the administration of medicine by the mouth he vomited once. The pain continued and increased in severity until October 25, when it was somewhat lessened for the next three days, but on October 28, the day before admission, it returned with renewed violence. The temperature on admission was 100° F., the pulse was 120, and the leucocytes were 16,000, increasing on the day of operation to about 18,000. General distention and rigidity of the abdominal walls was present, both distinctly more marked on the left side. There was a doubtful impairment of resonance with slightly increased resistance and tenderness over the usual site of appendicitis as compared with the more central portions of the abdomen. A left-sided mass was continuous with a median area of dullness which proved to be the bladder. Withdrawal of nine ounces of urine with a catheter removed this median dullness, but the left sided mass remained. My assistants believed that they had detected per rectum a right sided pelvic induration and certainly peritoneal

PLATE LIV.

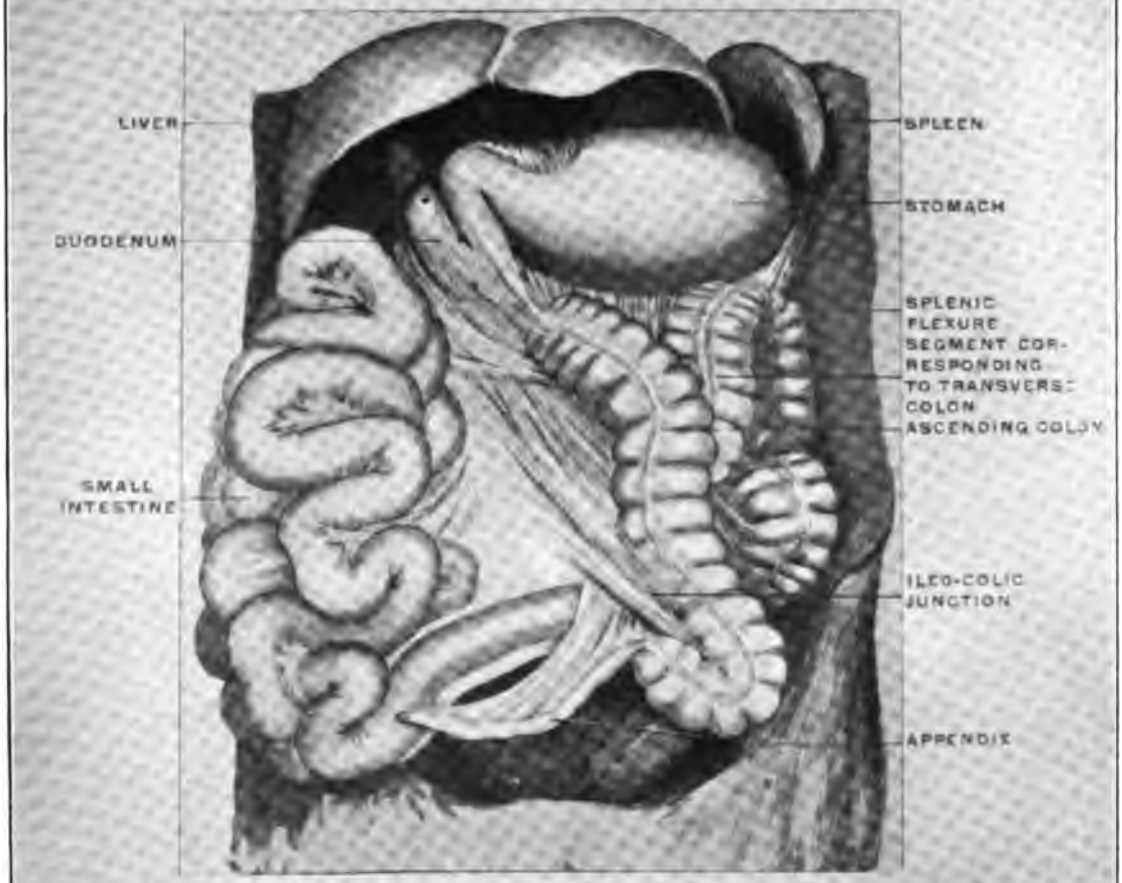

FIG. 118.—Abdominal viscera of adult human female, in a case of arrested rotation of the intestines. (Columbia University Museum, Sinly Collection.)

2. For diagrams of a number of these see an excellent article by Carl E. Black in the Annals of Surgery, Vol. 56, page 880.

tenderness in that situation. Under anesthesia the problematical right sided dullness on percussion and mass could not be certainly verified, but was believed probably to have been caused by the tense condition of the parietes; the left sided mass was now more readily detected.

Every operator occasionally meets with cases of appendicitis where the tip of the organ crosses to the left side of the abdomen, or at least the main inflammatory focus seems to be located in this region when first examined by the surgeon. Of course with complete transposition of the viscera, which is rare, appendicitis should be left sided, but a left sided appendicitis is more often spoken of than seen, this condition being somewhat simulated by a suppurative diverticulitis. This latter disease however, does not give rise to confusion in young children because the precedent pathologic alterations of the colon wall are not believed to occur in early life, these being more usually seen in adults, especially in middle life or advanced age. One would think the last word has long since been said about appendicitis, but the importance of recording cases like my own lies in several facts. First, when a right sided source of inflammatory abdominal trouble is not clearly indicated by the detection of a mass in this region by external palpation or rectal examination, while a left sided induration exists, any exploration must be attempted by such a method that by suitable modifications, both sides of the abdominal cavity can be reached. Again, when search in the right inguinal regions and hypochondriac regions, in cases diagnosed as appendicitis does not promptly enable the operator to locate the caput coli, or an inflammatory mass, search should at once be made on the opposite side. In my case a distended rigid condition of the abdominal walls rendered an accurate examination difficult, while the reported detection of a right sided mass by palpation and per rectum obscured the diagnosis. Still further, a greatly distended bladder fusing with the left sided mass was open to the possible, although un-

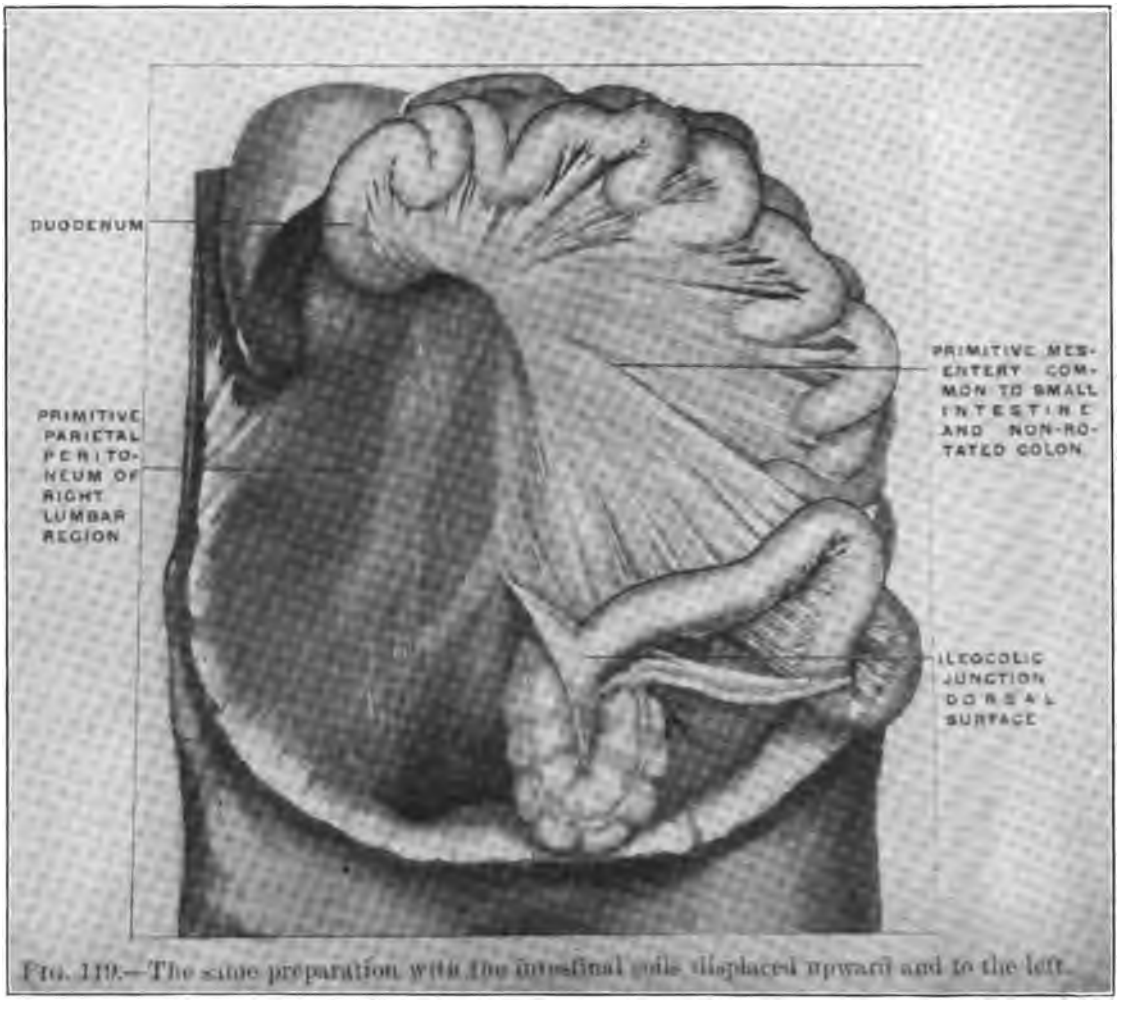

FIG. 119.—The same preparation with the intestinal coils displaced upward and to the left.

(Columbia University Museum, Study Collection.)

likely, explanation that this organ had been incorporated with an inflammatory mass and dragged over, the trouble originating in a normally located appendix with its tip extending sinistrally across the abdomen.

My first impulse therefore to make a left sided incision was resisted, and a right sided one splitting the rectus was made. Search for a normally placed caput and appendix was rapidly completed, only somewhat congested coils of small intestines being found, even normal omentum being absent on this side. Per contra, on the other side the usual mass of omentum adherent to everything in its neighborhood was found, imprisoning the caput coli with a perforated appendix surrounded with pus, containing a loose concretion.

While it was not so easy to conduct the subsequent manipulations as if the incison had been made more to the left, a satisfactory operative result was secured, the steps of which will not be detailed because they are of no particular interest. A careful study of the relations was readily made out, the caput occupying the same position in the iliac fossa as it usually does on the right side, the ileum entering normally, the usual amount of this intestine filling the true pelvis. The colon ascended upwards towards the spleen if it did not actually reach it, seemingly forming a splenic flexure instead of an hepatic one. Not wishing to infect the remainder of the abdomen by free handling in the presence of pus, the relations of the splenic and hepatic flexures, and the transverse and descending colon were not made out exactly, but as far as observed were otherwise normal although displaced so as to simulate partial transposition, but a study of the exact conditions shown by the illustrations reproduced from the actual conditions found in cadavers

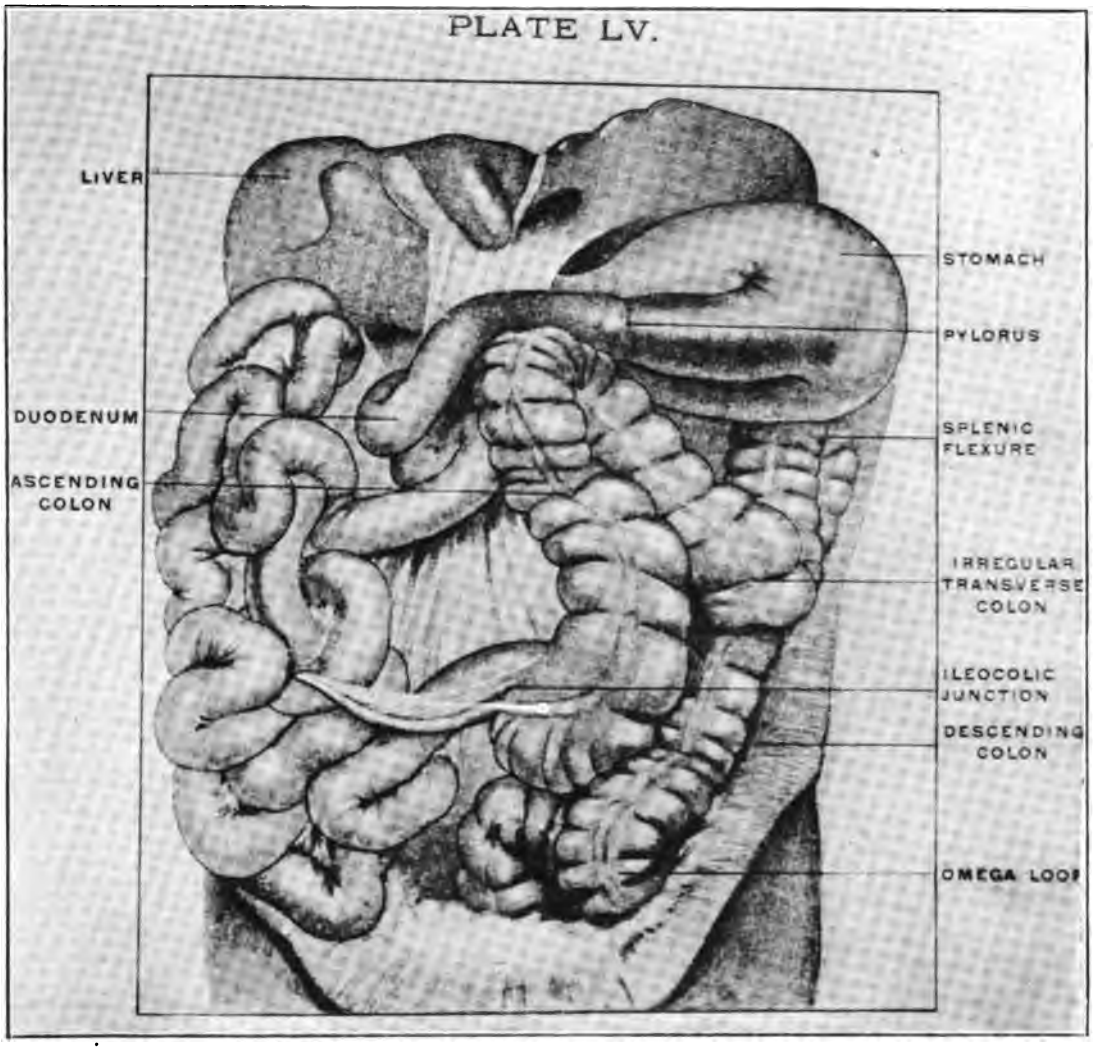

Fig. 120. Abdominal viscera of adult human male; non-rotation of intestine. (Columbia University, Study Collection.)

show how readily I may have been deceived, except as to the relation of the caput, appendix, and ileum.

Figs. 118, 119, 120, 121 will show the conditions presented by non-rotation of the colon in the adult, while Fig. 123 shows non-rotation of the cecum yet with the appendix in the right iliac fossa. Fig. 122 shows what was very possibly the condition in my case, contrasting well with the almost normally placed appendix although the rotation of the cecum was partially arrested. The perfect or imperfect rotation of the cecum doubtless accounts for some of the common locations of the appendix which are too often described as abnormal.

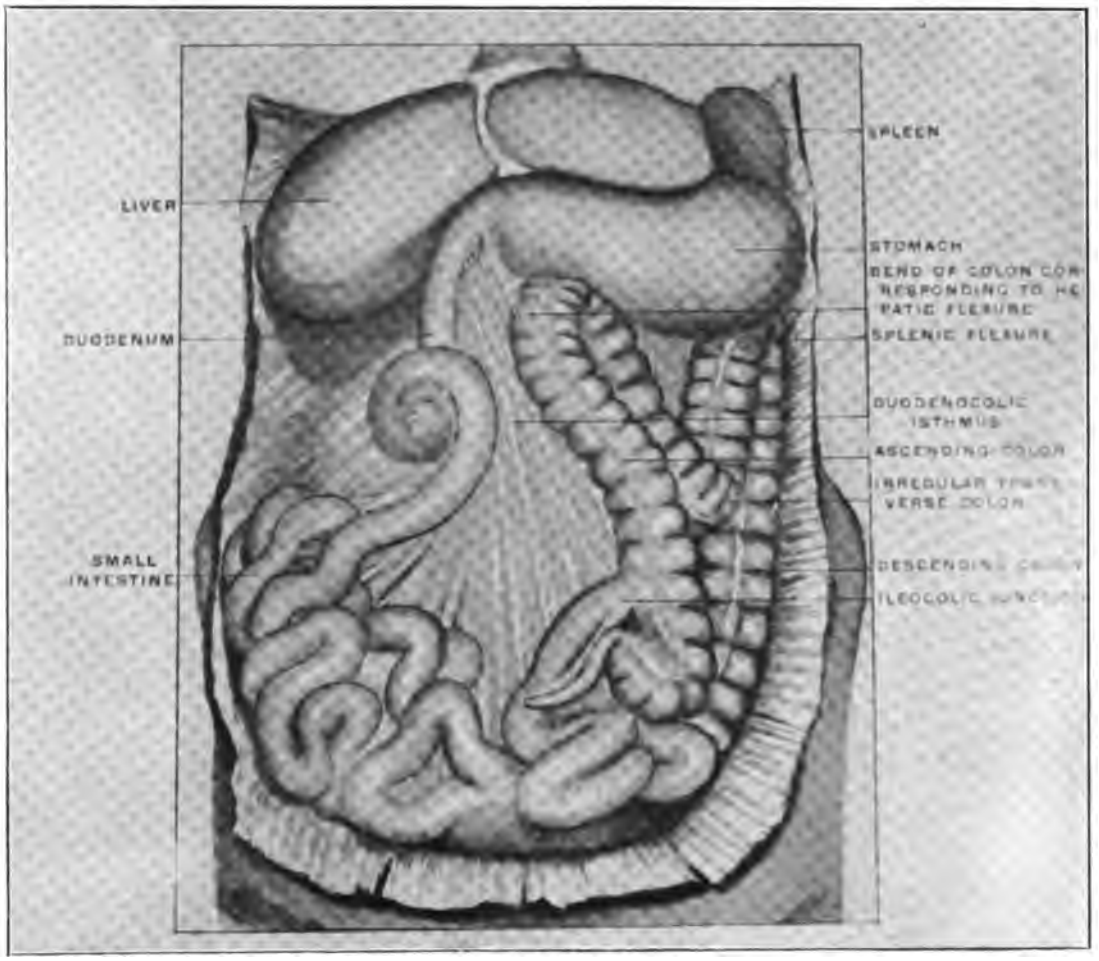

Fig. 121. Abdominal viscera of adult human male; non-rotation of intestine. (Columbia University, Study Collection.)

DISCUSSION.

Dr. Walter A. Hoyt: This certainly is a very interesting case, and emphasizes the desirability of taking a careful genitourinary history, not alone to rule out any disturbance of the genitourinary tract, but to enable one to make a better diagnosis of abdominal conditions. I saw this patient when he first entered the Hospital. Examination at this time showed a mass in the left side. Percussion over the right side revealed some dullness. Examination per rectum revealed a cystic mass. The patient had been taking morphine and complained of no pain. However, on careful inquiry it was found that the patient had not passed urine for the last thirty-six hours. The patient was catheterized, and about ten ounces of urine drawn off. Subsequent examination revealed no mass in the rectum, and the dullness on the right side had disappeared. Apparently the distended bladder had been the cause of the right sided findings, a fact which should always be taken into consideration in other obscure cases. One other interesting point is the efficiency of an exploratory incision. Through a right rectus incision it was possible to attend to all conditions arising in the left side of the abdomen, which as had been shown extended well into the iliac region. From the first, the patient did not drain well, although a tube drain was placed in the main incision, and a counter drain placed in the left side. Bichloride dressings were applied, but did not bring about an increase in the drainage. On the third day when a great deal of drainage should have been present, there was none at all. The tube drains were syringed out with sterile salt solution, and it was found that both tubes were blocked by broken down tissue and pus. The patient straightway started to drain, and had no further trouble. The patient's recovery after this was uneventful, and he was discharged day before yesterday in good condition.

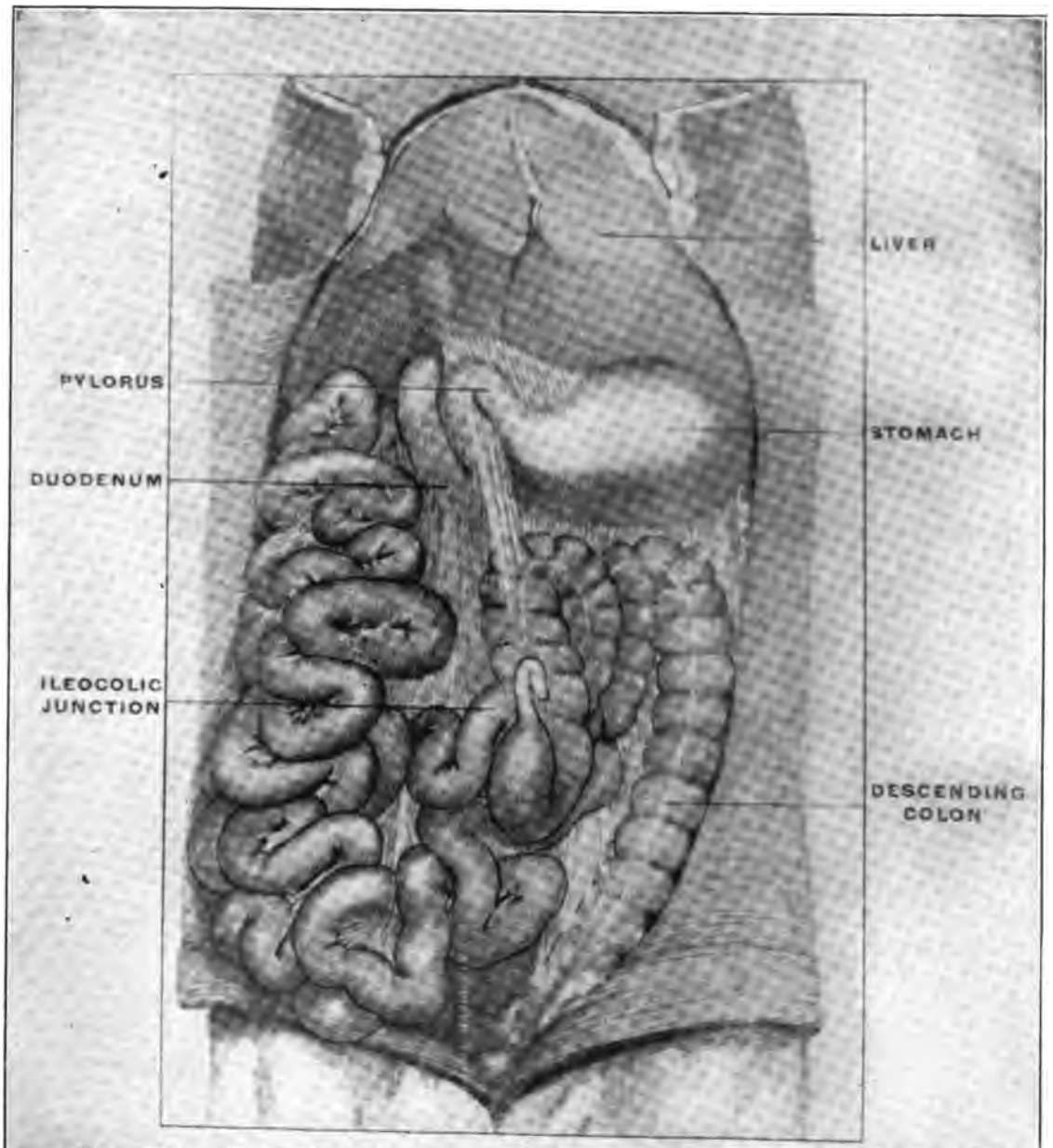

FIG. 122.—Abdominal viscera of child, two years old; non-rotation of intestine. (Columbia University Museum, Study Collection.)

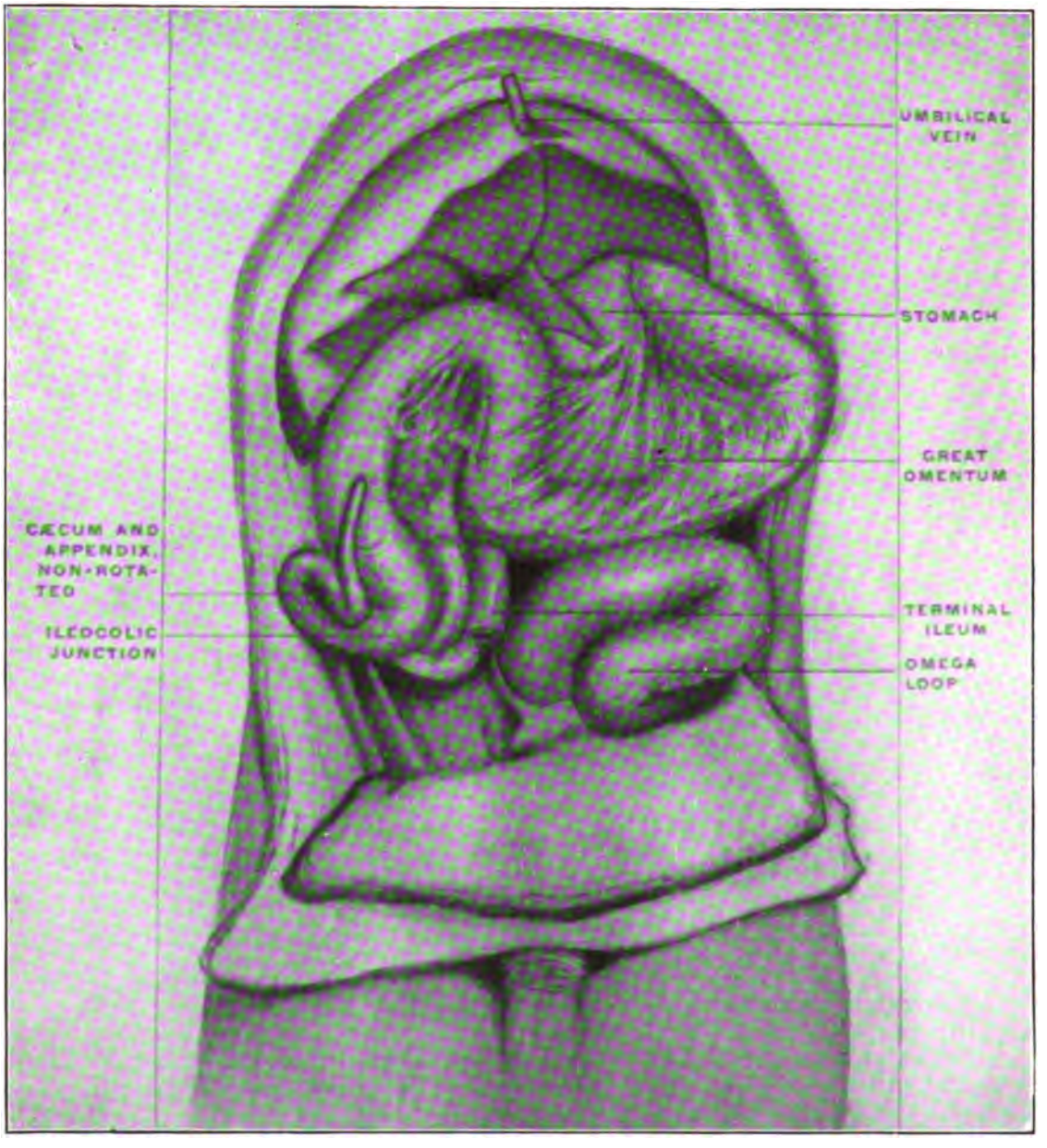

Fig. 123. Human foetus at term; abdominal viscera, hardened in situ; non-rotation of the caecum. (Columbia University Museum, No. 1813.)

WOUNDS OF THE FEMORAL ARTERY.

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My first real intimate acquaintance with a wounded artery of the lower extremity took place several years ago under the following peculiar circumstances. The owner of this artery, a young man of twenty, was standing on the sidewalk in his home town. It was the evening of the Fourth of July and the town, though nearly bursting with patriotism, did not possess a cannon.

The people were able to make an old fashioned noise by firing an anvil. More noise was desired and the noise could be increased if the hole in the anvil could be made to hold more powder. To meet these indications, the hole was prolonged by using a nut such as holds the wheel to the axle on a lumber wagon. This hole was filled with powder and the noise was a success but the force of the explosion tore the nut in pieces, all but one piece passing harmlessly away in the air. The important piece came toward the young man on the sidewalk, struck the median flap of his trousers and entered the flesh above and to the left of the pubes.

The size of the projectile and the depth to which it had penetrated the tissues was a matter for speculation, as only a small wound appeared upon the surface, where the soft parts had at once closed around it so that a probe, when inserted, did not come in contact with the metal.

The hemorrhage, at first sharp, was soon controlled by an antiseptic compress and the patient was placed in bed in a recumbent position where he remained for a week without any unusual happenings. About the eighth day when he arose to a sitting position as he had done before, there was a sudden gush of blood from the wound, which ceased, however, as soon as he again resumed the recumbent position.

The same accident happened again later in the day and I was called by his physician. The leg was cool and a little swollen but no signs of infection were present. There was no sign of pulsation in the femoral artery below Poupart's ligament, so I decided that the iliac externus was wounded and that the missile blocked the opening or pressed upon the vessel.

I enlarged the abdominal wound upward until I could introduce my finger, feel the relation of the missile to the vessel, also compress the vessel above the wound with my finger below the vessel and my thumb on the skin outside. Thus prepared I removed the piece of iron. At once, there was a large spurting stream of blood, which, owing to my being prepared, was easily controlled, but at the same time confirmed my suspicion of a wounded iliac artery. I directed my assistant to cut down upon the vessel below my point of compression and ligate it. This was easily accomplished and the hemorrhage was completely controlled.

I did not ligate the vessel below the point of injury because it was already plugged with a clot eight days old and would be safe unless disturbed by infection. Also I did not wish to invite infection by disturbing the wounded tissues more than was necessary. I thought this an unusual condition at the time, a missile tearing a hole in a main artery, entirely blocking the wound, thus preventing severe hemorrhage and at the same time completely shutting off the circulation below. The treatment was unique in that a wounded iliac artery was ligated above the wound only, to control hemorrhage.

The missile was one half of the large nut that had been used to increase the length of the hole in the anvil. Collateral circulation had been so well established during the week preceding my ligation, that recovery took place without disturbance to the leg.

Another important experience was with the femoral artery in 1898, when A. A., a lad of 16 years, entered the University Hospital because of an arteriovenous aneurism on the right side about four inches below Poupart's ligament. This pulsating tumor followed an injury incurred five years before by accidentally plunging a sheep shears deeply into the thigh, wounding at the same time both artery and vein. The wound was dressed and the patient was placed in bed. He seemed to be making a good recovery but two weeks after the accident he got up and walked a little. While returning to his bed he had a sharp pain at the seat of the wound. He felt a buzzing sensation and soon discovered that a swelling as large as an orange had formed at that point. He remained in bed about one month longer and the tumor diminished in size. When he entered the Hospital it was larger than a hen's egg and a distinct thrill could be felt in the large veins of the leg as well as in the tumor. Both artery and vein could be felt pulsating above the injury.

He walked on this leg for nearly five years and probably would have continued at his work as a farm laborer if an ulcer had not appeared one month previous on the inner and lower part of the thigh as a complication. This ulcer not only refused to heal but grew larger. As it was in the immediate neighborhood of pulsating veins, he had been warned, that these might break at any time and result in death from hemorrhage. This brought him to the Hospital and he came expecting an amputation,

but was willing to accept ligation instead, or any operation, which might save his leg.

In January, 1897, Dr. John B. Murphy of Chicago, published in the Medical Record a number of experiments on the surgery of the arteries and two operations upon the femoral vessels. These reports were very inspiring and contained the first known successful end to end suture of a severed artery.

His first case was a wound of the internal saphenous vein which was closed by continuous suture. The femoral vein was also injured and sutured in like manner. The femoral artery was not sufficiently damaged to require operation, although a piece of its surface was torn. The wound healed, but one week later a tumor formed, which had to be opened and a clot four inches long turned out. The femoral artery was found to be eroded for more than an inch on its inner side and resection of this vessel became necessary. About one inch and a half was removed and the ends ligated. Two ligatures were applied above and one below.

The second case reported at the same time was a gun shot of the femoral artery, causing an aneurismal tumor. This was operated three weeks after injury by resecting the vessel and suturing the ends together. The wound in the artery was three-eighths of an inch long and one half inch was removed. The proximal end was inserted into the distal end and sutured in place. The femoral vein was also sutured. The patient is said to have made a good recovery.

I had a vision of suturing the vein in my case but did not finish it that way. An incision about six inches long was started just below Poupart's ligament and carried over the tumor in the line of the vessel. My dissection first exposed the vessels above the tumor and a ligature was carefully placed around the artery and another around the vein for future use.

The vessels were then exposed in like manner below the tumor and ligatures placed ready for tying. The tumor was then exposed but the vein was greatly enlarged and the relations to the artery were so intimate that I was obliged to tie my ligatures and remove the sac. The patient was put to bed with the leg elevated and well protected with cotton for several days. At the end of two weeks he was allowed to let it hang down for a short time to test the circulation and when he left the Hospital it was in good condition. This leg had five years' preparation for a feeble circulation and bore it well.

Another patient with injury to the femoral artery, Mr. B., of Battle Creek, was admitted to the University Hospital, June 22, 1913.

He was twenty-five years old and gave the following history concerning the formation of a tumor on his right leg: Three weeks ago, while repairing a shoe with a pocket knife, the knife slipped and the blade, which was about one and one half inches long, entered full length into the right thigh on a line of the femoral artery above Hunter's canal about five inches below Poupart's ligament. The immediate hemorrhage was stopped by tying a rope tightly around the limb above the point of injury. When the rope was removed it was dressed with a compress and a tight bandage. This dressing remained in place three days, when it was removed and was replaced by a similar dressing, which was allowed to remain for the same length of time. The whole limb was swollen and painful, but there was no suppuration, and the wound healed without signs of infection.

Present condition: The whole extremity is swollen and the patient is unable to walk. There is a tumor about the shape and size of a pear and the surface is reddish purple in color. There is a scar on the most prominent point which shows where the knife entered the thigh. Pulsation can be felt in the veins in the vicinity of the tumor and a distinct bruit or thrill is very pronounced in the tumor itself. There is a numbness below the wound, which extends well down the inner side of the leg. The tissues are tender and sore and the patient complains greatly of pain which seems to radiate from the tumor.

Diagnosis: Aneurism of the femoral artery, due to a knife wound of that vessel.

The patient was placed in bed with the limb elevated and was carefully watched for three days to see that no suppuration was pending, also to favor the reduction of the swelling. The leg had been injured sixteen months before in a railroad accident and the patient informed us that some swelling from this accident remained when the present one occurred.

With rest and elevation, the swelling decreased but the tumor remained as prominent as ever. The operation was performed on June 25, 1913, four days after the patient entered the Hospital. After the usual cleansing, the femoral artery was exposed about three inches above the point of injury and a Crile clamp applied with sufficient pressure to prevent any flow of blood. About two inches of the artery was exposed below the tumor and another clamp was applied. The tumor was then opened and the wound in the vessel exposed. The laminated clots, which formed the walls of the sac were carefully removed until healthy tissue was found. The wound was little more than half an inch long and directly in the line of the artery. There was no enlargement of the vessel at this point but the edges of the wound were nearly one twelfth of an inch apart in the middle.

After removing all of the clot and the newly formed tissue, the edges of the wound of the artery were freshened by scraping with a nar-

row sharp knife. An attempt was then made to suture the wound by using a very fine needle and white silk such as is put on the market by the supply houses for that purpose, but this was a failure. We were not successful in passing the first stitch because the needle broke. We sucsucceeded in passing the stitch with a second needle, but in tying it the thread broke. These were then discarded for the fishhook needle and ordinary fine black silk thread and we were able to place and tie all the necessary stitches without breaking either thread or needle. Five stitches were employed, they were placed well back from the edge of the wound and passed through all of the coats except the intima. In tying each suture care was taken to approximate the edges of the incision without unduly narrowing the vessel. The lower clamp was then removed and the blood allowed to enter the vessel from below. There was slight oozing from one point which ceased after sponge compression for five minutes. After waiting fifteen minutes for a coagulum to form, which would seal the vessel before full pressure of the blood stream from above was allowed to enter, the clamp was partially loosened, the blood flowed through and there was no leakage. Before the clamp was entirely removed, the sheath of the vessel and the adjacent tissues were closely folded around the point of injury and sutured in place with fine catgut. The skin was sutured up to the upper Crile clamp and this was removed some time later.

There were some bleeding points at the upper angle of my incision so deep that an extension of the incision would be necessary in order to ligate them. Instead of doing this, the hemorrhage was controlled by two forceps which were left in place and the upper part of the wound was left open for the following reasons: To allow the forceps to remain on the vessels, which could not be ligated: To readily detect any leakage from the repair; to allow drainage of damaged tissues, which might easily become infected and in turn infect the vessel wound if fluids were allowed to accumulate in contact with the sutures; Last of all that the vessel could be promptly secured in case of secondary hemorrhage.

The patient was put to bed with the limb flexed in a comfortable position and the knee supported upon pillows. When the patient became very tired and suffered pain because of the fixed position codeine was given. The forceps were removed at the end of twenty-four hours. The loose packing was removed on the third day and the wound closed. From this time recovery was uneventful. The temperature arose to 101 on the third day and remained at that point but a short time. Pulsation was good in the posterior tibial artery, which showed that the operation was a success. Twenty-one days after operation, he was allowed to walk about and left the Hospital July 22, just one month after entering.

Here are some of the lessons which I learned from this operation: That any accessible wound of the large vessels can be repaired by using an ordinary fine needle and thread. That the required material which is furnished by the trade may do very well for laboratory purposes but cannot always be depended upon in actual practice. That the formation of clot will help to seal the slight remaining wounds if the clamp is closed and compression is maintained over the point of leakage for a longer time than is ordinarily required for the coagulation of blood. That the upper clamp should be slowly and carefully released after the rest of the wound has been closed. In a doubtful case, a provisional ligature should be left in place on the vessel above the wound, which can be closed or tied immediately in case of severe leakage.

The pathologist reports that the tissues from this case, particularly the inner layer, have the appearance of the walls of an abscess. Trichinae were also found in these tissues.

Wounds of the femoral, though frequently seen in military surgery, are of rare occurrence in private life. Bryant and Bucks surgery published in 1910, reports twelve cases of suture of lateral wounds of the femoral alone. If other cases have been reported in this country since that time I have failed to find the reports. There are very few cases of arteriovenous aneurisms of the femoral reported. Lund of Boston in 1908 reported a case of stab wounds of both femoral artery and vein, which were successfully repaired nine days after the accident. Sherman of California reported a similar successful case about the same time. Both of these cases had a double injury to the artery and one to the vein, the knife being carried through the artery and into the vein.

G. T. Vaughan of Washington D. C., in 1910 reported a double wound of artery and vein three inches below Poupart's ligament, which was repaired eighteen days after the accident. Though the vessels were diminished in size by the repair the recovery was good with pulsation.

Quite recently a number of attempts have been made to cure gangrene of the lower extremity, or at least prevent its extension by establishing an arteriovenous circulation in the femoral region. San Martin was the first to try it by making a lateral anastomosis between the femoral artery and vein. Hubbard in 1906 made an end to end anastomosis of artery and vein but without success. Muller of Philadelphia, collected ten cases in which the operation had been done in various ways with poor success.

These attempts, though many failed, have

developed some good ideas about the methods of operating. McMillan and Stanton of Schenectady found by sad experience that wide separation of a vessel from its sheath might result in necrosis of the vessel itself.

Mattress or continuous sutures may be employed according to the conditions of the parts or the fancy of the operator. The continuous suture is employed not only to repair lateral wounds of the artery, but circular cuts and resections as well.

Ordinary sewing needles straight or curved, may be used provided they are not too large. Fine silk, white or dyed is commonly used. The white is preferred because the dyed silk loses its strength in the process of coloring. Catgut has been discarded as it absorbs too soon for safety. The threads may be smeared with sterile vaseline, to make them run smoothly and to prevent kinking. The vaseline may also be applied to the repaired wound, to fill small openings and favor the formation of small clots.

Of all the blood vessels the femoral artery is best fitted for surgical operations. While its exposed position makes it liable to injury, it is accessible and easily repaired. It has the thickest walls of any vessel except the aorta. It is more frequently injured than any other of the large vessels except the axillary and has a larger number of successful repairs to its credit than that vessel.

Much that I have said concerning surgery of this artery applies equally well to the other vessels.

DISCUSSION.

Dr. Conrad Georg, jr.: I desire to compliment Dr. Darling upon his brilliant success with this operation. I have had similar experience in my experimental work upon the suture of bloodvessels. First the needle and then the sutures would break and the latter were very difficult to tie, so I can appreciate the difficulty that Dr Darling had with this operation. I spent about two hours in suturing the common carotid artery of one dog to the external jugular vein of another in an attempt to perform a direct transfusion of blood. Furthermore, this operation confirms the opinion I have always held, as a result of my experimental work upon the bloodvessels, that if I should ever perform this operation upon the human being I would use a stronger suture than that recommended by Carrel and Guthrie for experimental work upon dogs. In the human being we have larger vessels to deal with and a stronger force of blood stream than in dogs, which these sutures must resist and a small suture will not stand the strain. The needles I have used for this work are the No. 12 Kirby needle, which is much smaller. I had difficulty in purchasing the latter needles as none of the wholesale houses in New York or Philadelphia had them. Eventually I had to send to London, England, where they are made. These needles are the smallest I have ever seen and will break in your hand if you exert very much pressure upon them. The operation of suturing bloodvessels is an extremely difficult one. The suture which does not include the intima is the preferable one where it can be used. As the technic of end to end anastomosis is slightly different from lateral suture I will describe it. In the first place the vessel is prepared as Dr. Darling did by putting on Crile clamps or some similar instruments protected with rubber to stop the flow of blood through the artery while it is being repaired. Great care is necessary in doing this for fear of injuring the intima which is fatal to the operation. The vessel is then cut through and all blood clots washed out with normal saline solution. Next the adventitia is grasped with a fine pair of forceps drawn over the end of the vessel and cut flush with the end when it will retract and leave the end of the vessel clean for suturing. None of the adventitia must be allowed to come between the sutures as it will result in the deposition of fibrin and the formation of a thrombus.

I would like to mention two cases of bloodvessel suturing which have recently been reported in the literature. The femoral artery was not among the vessels operated on, but the principles are the same. In the October number of the Annals of Surgery is a case reported by Dr. Sherrill of Louisville, Kentucky. It was a backward dislocation of the elbow accompanied by considerable swelling of the forearm and there was no pulse in the radial artery. A rupture of the brachial artery was suspected and even though the arm was immersed in hot water the collateral circulation was not established at the end of three hours. The surgeon, therefore, concluded that the patient would lose his arm unless a suture of the artery could be made. Incision was made to the wounded vessel which was found completely divided and the ends filled with blood clot. He reduced the dislocation and sutured the artery and the circulation in the arm was gradually restored.

There was another case recently reported by Danielson of Germany which is of great importance because it opens a new field for the surgery of the bloodvessels. Hitherto it has been supposed that the operation had to be done under aseptic conditions in order to prevent the much dreaded thrombosis with metasasis when operating in the presence of infection. Danielson, however, operated in the presence of infection and obtained a good result. The case was one of a stab wound of the axillary artery. The attending physician applied a tourniquet around the shoulder and sent the patient to a surgical clinic in another town, without having dressed the wound. It was five hours after the accident before the patient arrived at the hospital. The arm was cold and no pulse could be felt in the radial artery. Upon loosening the tourniquet the blood spurted out of the artery in a stream so that it was necessary to reapply the tourniquet. The surgeon then sutured the artery. The wound was drained because of the possible presence of infection. The next day the pulse could be felt in the radial artery. There was a high fever and a free discharge of pus from the wound which gradually healed by granulation. In this case there was no formation of a thrombus. That the results in this case were not due to the gradual formation of a thrombus and the establishment of the collateral circulation is proven, in this surgeon's opinion, by the fact that a pulse in the radial artery could be felt soon after the suture and continued afterwards. It thus appears that we can suture blood vessels with safety even in the presence of infection.

REPORT ON THE DEPARTMENT OF ROENTGENOLOGY, UNIVERSITY HOSPITAL, ANN ARBOR, MICHIGAN.

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I have been asked to report on the progress in the Department of Roentgenology. Having visited the place you are all familiar with the progress made in the matter of equipment and all have opinions concerning the character of the work we are doing. We prefer to let it speak for itself.

Progress is a relative matter and implies a starting point and a goal. We started where progress left off in 1906. For that time we had a good equipment. It was not extensive, but its quality and efficiency were good and adequate for radiography as it was then practiced. From that time, until June, 1913, progress was retrograde, both in the character of the work, and in the physical condition of the equipment. Repairs had been woefully neglected, and some valuable apparatus had thereby fallen into disuse.

In the mean time, the practice of roentgenology had made remarkable strides. This is partly due to a better understanding of the physical principles underlying the application of the X-ray, and partly to the improvement in apparatus. Seven years ago, the radiographer was limited by the shortcomings of his generators. This is no longer true. At the risk of being too technical allow me to explain.

The X-ray tube has distinct polarity and requires an undirectional current. Its resistance is very great and it requires a voltage of from 35,000 to 90,000 volts to excite it. The X light given off is a small fraction of the energy supplied to the tube, and relatively large currents are required for picture taking. It has lately been found that the penetration of the X light depends solely on the voltage maintained at the terminals while the volume of rays given off is a direct function of the current. The product of the voltage and the current measures the power consumed.

The static machine gives a perfectly undirectional current, but its power is limited by the fragility of the material from which it is constructed. Their efficiency is further reduced by their unreliability under varying atmospheric conditions.

The X-ray coil produces an alternating current. In one direction the impulse is of high potential, and low ampereage, in the opposite direction it is of low voltage and relatively high ampereage. The problem of suppressing the latter current is a very vexing one, which has never been satisfactorily solved. The "inverse current" has until recently been the roentgenologist's incubus. The coils themselves can be made in large sizes, but the output is strictly limited by the capacity of the interrupters, which are necessary with them.

The interrupterless transformer of today supplies an absolutely undirectional current and can be built in large sizes. Twenty horsepower machines have been placed on the market. No tube at present made will carry a load of such magnitude and six to ten horsepower appears to be our present working limit. With the interrupterless transformer we have an adequate supply of suitable current and we are placed in the position of being limited only by the capacity of the tube.

Two great obstacles to an extension of the radiographic field were everywhere recognized, the lack of sufficient power and the unfortunate necessity of using penetrating rays. Power means speed and shortened exposures. In 1903, when one and two minute exposures were the rules in a search for renal calculus it was admitted that only from five to seven per cent. were demonstrated on the plates. Today with half-second exposures an operator is dissatisfied with an average below 95 per cent. The explanation lies in the fact that movement of the calculus, respiratory and otherwise, is practically nil during so short an exposure, whereas with the old technic, its shadow was spread over considerable area and became lost. The principle is of course the same as that in photography where a long time exposure of a fairly busy street will give a picture free from either pedestrians or vehicles, while a "snap shot" will show them all in sharp detail. Radiography of the stomach and intestines were impossible, because the peristaltic movement could not be controlled. Intensifying screens were introduced some six or seven years ago, and were soon regarded as necessities. The early screens reduced the time of exposure to about one-fourth and they have since been improved to about twice that efficiency.

Less penetrating rays were very essential because they give vastly greater contrast in the radiogram. They make certain the demonstration of relatively permeable calculi and make possible a certain amount of soft tissue differentiated. Unfortunately, soft rays require greater volume, involve more inverse, more heating of tubes, and longer exposures. Between these alternatives the more penetrating rays were found more certain and more economical.

The introduction of the transformer has solved most of our difficulties. It delivers an absolutely undirectional current and can be built in any size units. It employs a form of current that allows of exact mathematical calculation and design. We are no longer limited

by our generators, but by the capacities of our tubes.

By the addition to our equipment of a 10 kilowatt transformer, several of the best intensifying screens and modern convenient accessories, we are in a position to undertake the work in any field which is now open to the radiologist and we only need greater skill in plate making, and better judgment in their interpretation to keep abreast of the procession in the diagnostic line.

To be sure, some of our devices are home made makeshifts, and a more liberal equipment would mean greater economy in labor and material, but we have the essentials, and a wider field is already open. Gastroentrologic examination with bismuth "per os" and "per anum" offers a wide field. So far the harvest has not been very great, but much good is bound to come from its careful and judicious tillage. Not only may the diagnosis of gastrocarcinoma be made with certainty in the vast majority of cases, but its position and extent may be more accurately gauged than by clinical methods. The differentiation of gastric and duodenal ulcers from other confusing conditions, is becoming more and more certain. Collargol injections of the urinary tract give valuable information in many conditions besides pyelonephritis, for example, tuberculosis, hypernephroma and certain anomalies. The greater contrast at our command makes possible greater detail in the cellular bones, in head work, and in the study of the mastoid and accessory sinuses. Periarticular structure can be fairly well demonstrated. Small differences in the density of the lung tissue are more certainly demonstrable.

But radiography is still largely an art, a matter of skill. We are still unable to measure and control our conditions so that results are infallible. Two recent inventions seem to promise just that. It seems probable that we shall be able to turn on just the shade of light, of just the candle power and for just the length of time that we wish. The first is the Cabot high tension direct current generator, which produces a ray of uniform penetration and therefore furnishes a theoretically ideal current for X-ray work, and the second the "adjustable penetration tube." Both are in the experimental stage, and soon to be put on the market. Already they have contributed a great deal to our knowledge of the physical laws underlying the generation and the properties of X-ray. Both are correct in principle and are bound to find their way into the best practice.

Another field with great promise for the future is that of radiotherapy. We owe to the scientific investigation of radium and the allied bodies a wealth of new knowledge concerning the nature and action of the X-light. During the last two years, an entire revolution has taken place in the technic and in the field of radiotherapy. Instead of the soft ray, for superficial lesions, the Freiberg technic now uses the hardest ray at its disposal for all conditions and a dose fairly accurately controlled by the use of a chemical indicator. It is now possible to gauge the dose to one-eighth of the quantity required to produce an X-ray burn. In practice three-fourths of seven-eighths of an erythema dose is given at a sitting and the dose is not repeated until the effects of the previous dose has worn off, usually from ten to fourteen days. The rays are carefully screened to absorb and remove all the soft rays before they reach the body. Deep lying lesions are approached from numerous directions by the "cross-fire" method. The results have been truly remarkable. Inoperable carcinoma of the uterus has disappeared without recurrence for one and one-half years. What the ultimate result will be the future only can tell. Carcinoma of the breast and stomach improve in many cases. Some are apparently cured. The field of gynecology has been invaded. Metrorrhagia is promptly controlled. Fibroids shrink in volume and cease to give trouble, pelvic adhesions are said to be absorbed. The literature is full of these subjects. The dermatologist is no longer the only specialist to use the X-ray with confidence and he uses it with far greater confidence and certainty of results than ever before.

Unfortunately, the whole issue has been seriously clouded by the coincident use of radium, mesothorium and similar bodies. The useful radiance of mesothorium has approximately eighty times the penetration of the hardest x-ray at present possible, but otherwise differs little in physical or physiologic properties. Hence we can easily understand the craze for hard and still harder rays. Improved apparatus and improved technic are certain to result to the great advantage of otherwise hopeless humanity.

I have tried to show our point of departure in the march of progress, our present position, and the ground we have covered, and if not the ultimate goal, at least the next mile post.

Radiography has been unscientific through ignorance, and has been the victim of exploitation by quacks and charlatans until it has lost caste with the older and more respectable branches of medicine. With more accurate knowledge of the forces handled and a more judicious selection of the tasks assumed, it will ultimately earn and receive a respect it has not hitherto deserved.

Inasmuch as the funds at the disposal of the Department for new equipment, and repairs will depend in no small measure upon the vol-

ume of business transacted by the Department, this feature becomes of some interest. It gives us pleasure to make the following comparisons:

In the calendar year 1911, 609 plates were exposed, with a gross receipt of $1,064.27. In the year 1912, 830 plates were made, with an income of $1,369.00. Since July first and including the whole of November, we have seen approximately 475 patients and 831 plates have been made with a net receipt of $1,220.90. In other words, in the past five months we have equalled the number of plates for the whole of the previous year, and have taken in slightly less money. For the greater part of that period, our equipment was still incompletely installed, and several lines of work we are now ready to undertake were not open to us. As our technic becomes more perfect, and we acquire new accessions to our equipment, our efficiency should further increase and the field widen.

Our motto is "We aim to serve" and to that end, we have introduced several innovations. We are keeping a four part cross index, which is at the disposal of any one connected with the Hospital. We can lay our hands on any desired plate in a very few minutes, or tell where the plate has gone if it has been borrowed. We have undertaken to give an unsolicited opinion on all cases referred to us for examination. We do not expect you to respect these opinions if they do not deserve respect, but we are not afraid to go on record, and ultimately hope to make them of real value.

We still stand in need of a number of important pieces of apparatus. We need more convenient rooms. Perhaps our greatest need is for a dressing-room with toilet. It is next to impossible to do colonic work without it. We need better and more economical apparatus for our photographic work. With the increase in the volume of cases needing treatment which present results seem to promise, we shall need more and specially devised equipment for this purpose alone. And if the work continues to increase as it has for the past few months, we shall certainly need more assistants.

We keenly realize our obligations to you for your co-operation. With your help we feel sure we can once more put the University of Michigan on the radiographic map where it belongs.

REPORT OF TWO CASES OF RICKETS SIMULATING LUES.

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The two patients I wish to present tonight are sisters, seven and five years old respectively. Both have marked deformities of the lower extremities, and the younger marked lumbar scoliosis. The general picture leaves no doubt but that both of these children have well marked cases of rickets. The deformed lower extremities, anterior bowing of the thighs, knocked knees, distortion of the tibiae, rosary, enlarged wrist joints, pot belly and the age at which the deformity began (time of walking) all speak for this disease. There are two points in each case which suggest the possibility of hereditary lues, namely—the marked

appearance of a saber shin and the scaphoid scapulae. The latter we not infrequently find in the Clinic and regard it simply as a stigmata of degeneration. The saber shin on the other hand is so characteristic of lues that we never can pass it by lightly. When we closely examine the older child we observe that in addition to the anterior bowing of the tibiae, there is a twisting of the bone to the inner side above the anterior bowing. This is not characteristic of a typical saber shin as may be seen in a typical case of hereditary lues in the Dermatologic Clinic. There are no other signs of hereditary lues in these children.

From the etiologic side we find some points

of interest. The older child was breast fed and seemed to develop well until she began to walk. Rickets is rare under these conditions. The younger child was fed on Mellin's, Eskay's food and crackers. This suggests a possible etiologic factor, but the mother says that the

milk she used was good milk. None of the early signs of rickets, such as head sweating, etc., were observed by the parents. The mother has had marked interstitial keratitis in both eyes for nineteen years. This developed about one year after marriage. The father gives no history of an initial lesion. There have been no miscarriages. One brother nineteen years old had knocked knees, but this is not noticeable at the present time. One sister fourteen years old is perfectly developed, but has slightly scaphoid scapulae. Wassermann reactions on father, mother and both children have been entirely negative.

The general deformities and bone changes are not characteristic of lues but the association of the two diseases is strongly suggested. The clinical evidence thus far, even in view of keratitis in the mother, which as I believe has been considered somewhat atypical by Dr. Wile and Dr. Parker, rather points to uncomplicated rickets.

DISCUSSION.

Dr. Udo J. Wile: Dr. Cowie kindly asked me to see these two children with him and I must say that my first impression was that both were examples of syphilis. On closer examination, however, and upon more mature study we found that the changes were probably not those of syphilis. The bowing of the tibiae anteriorly suggests syphilis it is true, but there is marked lateral deviation which is not found in syphilitic bones, which are not soft. These are essentially soft bones and mechanical factors have certainly been at work in producing these changes. Not only are the tibiae bowed in this way but the other leg bones are also malformed, particularly those of the thigh. The occurrence of interstitial keratitis in the mother also suggests that the change was syphilitic but the interstitial keratitis is not essentially of the type that one finds in syphilis. Dr. Slocum has expressed the opinion that the change could easily be from any one of a number of other causes. The Wassermann reaction on the father, mother and two children is negative. However, this should be regarded with reservation as speaking against syphilis because we have found occasionally that the mother of syphilitic infants frequently becomes negative during pregnancy. These cases are instructive in that one may have a condition simulating "tibia en lames de sabres" other than occurs in hereditary syphilis.

Dr. David M. Cowie, (closing the discussion): I have nothing further to add except to point out again that the majority of symptoms and signs in these cases are in favor of the diagnosis of rickets. The two diseases might easily be associated, and it will be of interest to study them further.

TRANSACTIONS
OF THE
CLINICAL SOCIETY
OF THE
UNIVERSITY OF MICHIGAN

STATED MEETING, JANUARY 3, 1914

THE PRESIDENT, R. BISHOP CANFIELD, M.D., IN THE CHAIR
REPORTED BY REUBEN PETERSON, M.D., SECRETARY

Reading of Papers

SUBPERICHONDRIAL HEMILARYNGECTOMY IN SQUAMOUS CELL CARCINOMA OF THE LARYNX.

R BISHOP CANFIELD, M.D.

Professor of Otolaryngology, University of Michigan.
(From the Otolaryngologic Clinic, University Hospital, Ann Arbor, Michigan.)

The extralaryngeal operation for the removal of laryngeal cancer, whatever the technic used has always resulted in the complete loss of the function of the larynx. The operation includes the removal of the larynx either partially or totally, turning the proximal end of the trachea forwards and suturing it to the skin, closing the communication between the pharynx and operative field and finally closing the neck wound either at the time of operation or later. This means that, for the rest of the patient's life, breathing must be accomplished through the neck, while the best voice that can be secured is an explosive whisper brought about by the sudden forcing outwards of the air contained in the mouth.

The purpose of this brief preliminary report is to suggest a method by which, it is hoped, in a certain number of selected cases of intrinsic laryngeal cancer, not only a satisfactory voice may be preserved, but also that breathing may be accomplished through the mouth. I have given to this method the name of subperichondrial laryngectomy. In brief, the technic includes a preliminary tracheotomy, incision of the perichondrium covering the thyroid cartilage and the subperichondrial enucleation of the thyroid cartilage together with the cancer.

This procedure leaves the space previously occupied by the larynx lined by perichondrium. After a partial laryngectomy the surface above and beneath this space will be covered by mucous membrane from the contiguous surfaces, while after a complete laryngectomy it will be necessary to cover this area with skin or mucous membrane grafts. The object to be secured is the patency of the tract from the buccal cavity to the upper end of the trachea. I am sure that this can be secured after a partial laryngectomy and am optimistic about it being possible after a complete laryngectomy, although in the latter case it may be necessary for the patient to wear a special intubation tube. The advantage claimed for the preservation of the perichondrium is that it assists in maintaining the patency of the tube and affords a surface over which epidermatization takes place readily.

CASE 1. Mr. H. R. M. age 69. The patient presents himself on account of a hoarseness which has been slowly increasing for about a year and a half.

Examination: The right vocal cord from the anterior commisure to the vocal process and the right false cord throughout a corresponding area is involved in a neoplastic process. The mass is rough on the surface and shows loss of epithelium over the anterior half. The posterior half is apparently covered by mucous membrane. The mass is pale, irregular in outline, covered with mucus and apparently infiltrates the neighboring tissues. Both arytenoids show moderate edema around their bases. Although the mass extends quite to the anterior commisure, the left half of the larynx shows no involvement when seen from above.

Operation, Dec. 27, 1913: Suspension laryngoscopy and removal of a specimen: at the time of the removal of the specimen, the base of the mass was found to be hard, rough and difficult to remove. A specimen was removed from the tumor, one from each arytenoid area and one from the left false cord.

Pathologic report: Specimen from the

tumor shows squamous cell carcinoma; other specimens negative.

General Examination: Chest negative except for moderate emphysema. Urine: Heavy reaction for reducing substance, moderate acetone.

In view of the fact that involvement of the left half of the larynx could not be demonstrated, a hemilaryngectomy was decided upon. Following a three day VanNoorden diet the patient became sugar free.

Operation, Jan. 1, 1914: Operation under novocain one per cent. anesthesia. (1% in 1-10,000 adrenalin). Median incision from hyoid bone to sternum, resection of the thyroid isthmus and preparation for low tracheotomy. Incision of the perichondrium over the anterior edge of the right thyroid cartilage. Separation of the perichondrium from the right thyroid cartilage. Tracheotomy. Incision of the cricothyroid membrane. Attempt to split the thyroid cartilage found impossible with scissors on account of the calcification of the cartilage. Thyroid cartilage finally split with Asche forceps. Separation of the two halves of the thyroid cartilage showed the tumor to be about the size of the first phalanx of the little finger. The left half of the larynx was seen to be apparently healthy. The cricothyroid and thyrohyoid membranes were then incised along the lower and upper edges of the thyroid cartilage. The greater wing of the thyroid cartilage was severed and the thyroid cartilage; the mucous membrane of the right half of the larynx and the tumor were removed in one piece. Two or three vessels were then ligated and the larynx packed with gauze. Two sutures were then passed through the perichondrium of the two sides but were not tied. Three sutures were used to unite skin edges. The operation was painless and without hemorrhage.

Post Operative Course, Jan. 11, 1914: For four days the patient enjoyed a satisfactory convalescence. Locally the condition was perfect. The wound did not become infected and but little mucus collected in it. With the edges of the incision held in coaptation a surprisingly good voice was secured. On the morning of the fifth day slight evidence of a pneumonic process was discovered over both bases behind. This process advanced with the tremendous rapidity sometimes seen in the terminal pneumonia of the aged and terminated in a few hours.

Autopsy: Moderate involvement of both lungs, fatty heart. Neck and bronchi negative.

DISCUSSION.

DR. C. B. DE NANCREDE: It has been extremely interesting to me, to hear this paper, because Dr. Canfield had the same experience in dealing with the thyroid cartilage that I had some thirty or more years ago, while operating for an intralaryngeal growth. The forceps would not divide the structure properly and I think I had to employ a Hey's saw. I think he is to be congratulated on having gotten so good a result, by infiltration analgesia, and I am very sorry my prognosis expressed the other day has been somewhat verified, I mean the chances of failure in diabetic cases.

NERVOUS CHILDREN.

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The title "Nervous Children" was chosen because we are not altogether justified in speaking of neurasthenia and hysteria as fully developed entities in the early years of life, as we observe them in the adult. The child presents only certain phases of these definite forms of disorders as they occur in the adult. This is self-evident from the fact that in the tender years of life we are dealing with an undeveloped psychic sphere. While certain characteristic symptoms of these disorders occur quite early in life we can not expect to find in a developing organism the symptom complex which characterizes certain definite forms of nervous disease in a fully developed psychic individuality.

The organic diseases of the brain and the spinal cord and the psychoses of childhood, also the hereditary psychopathic states, and the various forms of mental deficiency cannot be classed under the head of nervousness. As is well known, there are certain anatomic peculiarities of the nervous system of the child which necessarily give rise to physiologic and psychologic characteristics. The child's brain presents an undeveloped fiber system; many of the ganglion cells of the newborn are not of the fully developed type and show some of the embryonal character. Retrogressive changes in the nervous elements of the fully developed brain present clinical features which are not unlike the psyche of the child. In consequence we may accept, in part at least, the fiber and cell development as the basis of the child's psychic development.

While one is able to establish certain more or less definite stages in the psychic development of the child, there are great individual variations which come within the normal limits. In the beginning, the manifestations which constitute life in the newborn are wholly expressions of the subcortical function. In other words, all activities are accomplished without conscious impressions and are, therefore, reflex in character. Gradually from the simplest reflex manifestations the activities become more complicated and finally invade the cortical, motor and sensory spheres. When

the child begins to differentiate between objects held before it and with its own arm reaches out and grasps the chosen one, we are certain that the motor cortex is active and that there are conscious impressions. It appears that a certain equilibrium is established first before any marked consciousness enters into these actions. So it is with the speech, at first a mechanical jargon, which gradually becomes intelligible speech in which the higher cortical centers play a part. The child learns to walk at the age of one or one and one-half years without the aid of a fully developed active consciousness.

In the development of affectivity, at first most primitive, is the differentiation between likes and dislikes but as the intellectual development progresses this differentiation becomes more and more apparent through the various emotional manifestations (joy, grief, sexual emotion). The associations, that is, the power to think, are extremely simple and few. They are simple analogues, that is, the child will call every woman mamma and every man papa. It is very evident that only the most primitive analogous conclusions are possible. As the vocabulary is more enriched (according to Ziehen at one and a half years about forty words, at the end of the second year over two hundred to three hundred words), the ability for more extensive associations is increased. In the normal child the separate psychic qualities are, as a rule, comparatively uniform in their development. There exists a certain harmony in the psychic development of the normal child. However, there may be pauses in the mental development which, to be sure, are of short duration, one or more weeks, very rarely months. During these periods stimulations bring no reactions and urging is of no avail, the progress in mental development returns spontaneously. It is, therefore, not necessary to urge the normal child in its mental exercises and in the psychopathic child such urging is decidedly harmful. Careful observations will reveal that the child possesses a marked imitative impulse, an important factor in the rearing of children and in the development of pathologic tendencies. It is responsible for much that is frequently attributed to heredity. In fact, hereditary influence counts for little when we determine by careful analysis the origin of the elements that form an individuality with the normal child or the anomalies in the abnormal.

The apparent independent judgment of the child in most cases is but a representation of a figurative association complex which is quite evident in the first years of school instruction where there is a tendency to make a strong impression upon the child's mind of definite formulated rules and fixed conclusions. The child is therefore unable to give reasons for these conclusions, the result of independent thought. Of course the effort is also made to stimulate the child to draw its own conclusions and to formulate independent judgment. This is with some children successful within a limited field, but never in general. The child who makes wonderful progress in a special field, as in mathematics or languages and fails in less complicated branches is not infrequently of a psychopathic disposition and the unusual attainment, a psychopathic symptom; this is of importance in connection with the development of certain anomalies.

The child does not appreciate the significance of its own existence, its personality, its relation to the outside world. This is evident from the fact that the child speaks of itself in the third person until the third year. Even then recognition of personality is manifest in a very primitive manner in that the child no longer speaks of itself in the third person, that is, instead of saying "William wishes to have" it says for the first time "I wish to have." We are, therefore, unable to recognize personality in the child before the end of the third or fourth year, much less anomalies of personality before this period. It stands to reason, therefore, that a nervous disorder of personality cannot appear before this time. In a general way the impressions through the sense organs are after this time more fully appreciated and the correct interpretation of the more simple ones is evident of a wider association becoming more and more complicated as time goes on, until the highest psychic function is attained, when we may speak of the child's intelligence.

In the earlier months of life the child is less susceptible to stimulation. Not only is this true in the motor sphere but frequently stimulation of the sensory nerves is not perceptible to the newborn. There are a number of neurologic conditions peculiar to childhood. The tendon reflexes are more active than in the normal adult from the second month to the second year. The umbilical reflex which is frequently absent during the first weeks is later very marked. Not infrequently we can obtain the Babinski toe reflex in the second half of the first year. The conjunctival reflex is present at the time of birth. On the other hand, the blinking of the eyes is often not present until the sixth or eighth week. The pupillary light reflex is present from the time of birth, while the pupils do not react in accommodation until about the fourth week. The photophobia, present at birth, usually disappears within ten to twenty days. Fixing of objects within the line of vision occurs in the fourth or fifth week, but following the objects with the eyes is not observed until the

third or fourth month. The newborn is deaf and the function of hearing is gradually established until at the end of the third month there is fairly good hearing.

There are certain peculiarities of childhood under normal conditions which are of interest in the study of abnormal states. In the fifth, sixth, seventh and eighth year the child develops an extraordinary interest in its surroundings and asks numerous questions. This is not an expression of a series of association complexes but is more or less mechanical, so that a number of questions pertaining to objects closely related to each other follow in succession in a rhythmic manner. In the emotional sphere there is little control in early childhood and a more or less marked impulsiveness is always apparent. Ideas presenting themselves are executed without consideration or control. Very early the child is able to distinguish and appreciate the difference between agreeable and disagreeable situations and unsightly objects when this requires no great amount of intelligence. Herein lies the secret of discipline as it is ordinarily applied to children. The child does not consider its act from an ethical standpoint, but associates the act with the situation that follows, be it praise or punishment, and here again comes into play the strong imitative impulse of childhood. The disposition of the parent and the situation created by the parent in the discipline of children are largely responsible for the disposition of the child. The proper punishment applied at the proper time will develop a substantial control in all of the child's acts, while praise has a tendency to increase the natural impulsiveness. Many of the anomalies of disposition and symptoms of nervousness are the result of mistakes in discipline in early childhood. It is of interest to note the well marked imaginative power of the child. It not infrequently mingles the imaginary with the real, which is evident in the susceptibility to fairy tales and phantastic portrayal. The memory of the child is in some respects peculiar. While the child generally has a quick conception, there is a tendency to forget on account of the lack of proper association. Nevertheless the psychic impressions of childhood are permanent, although apparently unconscious, and are therefore not memory in the ordinary sense. Most of the associations that can be reproduced under certain definite stimuli are those of childhood impressions. Observations and experiences have a permanent place in the unconscious mind, and if of a painful character they again may be reproduced in a distorted form as nervous symptoms.

ETIOLOGY.

In the majority of nervous children one is able to demonstrate a certain endogenous predisposition, the so-called psychopathic or neuropathic disposition. But in studying the personality of the father, or the mother and perhaps the several other children of the family, as well as the general environment of the child, the endogenous predisposition does not appear so prominent as a causative factor of nervousness. Many times the neuropathic disposition is an acquired complex of nervous manifestations, the result of environment. However this may be, it is true that the resistance of children to outside influences at the time of birth is just as variable as their external appearance. One child becomes easily nervous, another less so, a third under the most careful regulations is predestined to be a nervous child. Among the avoidable exogenous causes of nervous children are the mistakes of early training, involving the personality and situations created by those having this responsibility, in which the physician is frequently a prominent figure.

Faulty training of children begins immediately after birth. A child in the first days, weeks and months of life requires a great deal of sleep, in the first week at least twenty hours in the twenty-four and for months after sixteen hours. There are many conditions too numerous to mention here that prevent this, even in the best regulated homes, but all of them avoidable. At this time these outward influences are only reflex, since, as already mentioned, there are no psychic impressions at this period of life. Later the usual method of amusing the child is unquestionably harmful. The small child should be lonesome and not subjected to the stimulations arising from the implements we choose to call toys.

The over stimulated child, the unusual child or the wonderful child frequently is a nervous child. It is often pathetic to hear the mother boast that her child can read at three or four years or can produce melodies after hearing them for the first time. Such children are frequently more or less exhausted by the time they reach the school age and are not equal to the demands made upon their neural resources. When the problems of the school curriculum become more difficult, there appear periods of exhaustion, irritability, disturbed sleep, et cetera.

Corporal punishment in childhood is a barbaric method of training. It is no longer permissible in punishing criminals, why should it be tolerated in the training of children? The normal child may survive with an amiable disposition, while that of the nervous child is surely not improved by such treatment.

The desire for freedom is an early manifestation in the child's emotional sphere and any forced restrictions will invariably produce re-

actions of resentment. When it is necessary to apply force there is always an error of training or in the disposition of the parent. It is therefore unnatural and unfavorable for the physiologic development of the child to be surrounded by and compelled to follow severe regulations in the home or in the school. An equilibrium can be established only by carefully observing the reactions of the individual.

Of the greatest importance in this connection are the physical and psychic trauma which not infrequently arise as a result of this form of applied force. The effect of a physical trauma and also of the psychic, to a certain extent, is the same as in the adult, resulting in a pathologic reaction in any psychopathologic individual. The majority of cases of hysteria in adult life have their origin in this period and from this cause.

In grouping nervous conditions of childhood the writer has chosen the plan of Cramer[1], who collects the symptoms under four heads as follows: neurasthenia, endogenous nervousness, complicated endogenous nervousness, and hysteria.

NEURASTHENIA.

In childhood, as in the adult, there is an exhaustion of the cortical nerve centers which occurs in children who are not necessarily of a neuropathic disposition, and is the result of strenuous mental effort without sufficient time for recuperation in rest and sleep, and which results in a chronic exhaustion of the brain centers. This type of disturbance undoubtedly forms the smallest number of nervous children. In two hundred cases of nervousness observed by the writer, there were but nineteen that could be thus classified.

ENDOGENOUS NERVOUSNESS.

This is a nervous exhaustion in a child with a marked neuropathic disposition and follows a moderate mental exertion in one who has the requisite amount of rest and sleep for a normal child. In other words, it has to do with a child with diminished resistance who has not the endurance of the normal child under normal conditions. This class was represented by twenty-eight in two hundred cases, the ages of the patients ranging from six to thirteen.

COMPLICATED ENDOGENOUS NERVOUSNESS.

This form of nervous affection is due to physical ailments in predisposed children. In this class belong the intensely nervous, sensitive, excitable, irritable, restless child ever prone to habit spasms, nocturnal incontinence, et cetera, yet who may show no actual evidence of nerve exhaustion. Among the more common causes are enlarged tonsils and adenoids, eye defects, diseases of the skin, disorders of digestion, constipation and incipient tuberculosis. In the writer's series there were ninety-three belonging to this class.

HYSTERIA.

Here the child presents a marked neuropathic disposition which is most evident in hypersuggestibility, increased imaginative power and inclination to lability and emotionalism. The physical stigmata are apparently not so numerous in childhood as in the adult. Anesthetic conjunctivae are frequently met with, as well as areas of anesthésia and hyperesthesia. When these are demonstrated they are sharply circumscribed and usually located on the back, thorax and abdomen. Seventy of the two hundred cases recorded were classified as hysteria, the ages of the patients ranging between four and fourteen years. Fifty-eight of these patients were girls.

The physical expression of hysteria in childhood is monosymptomatic, at least one symptom is so apparent in the patient that it overshadows all other manifestations. It is very rare that a more or less complete symptom complex is observed in children before the age of ten. Sensory and motor anomalies are about equally divided, the psychic manifestations being always present. The cases under analysis presented a great varity of psychic anomalies, some of which I will briefly mention: A patient with a perverse paradox mental reaction was repeatedly overcome by fear which was followed by nausea and vomiting whenever she saw a certain shade of red, the result of a previous experience in suddenly coming upon a bleeding animal while out walking. Dislikes for certain odors and tastes ordinarily pleasing to the normal child were observed in several patients with somewhat similar explanations. Fears and timidity resulting from sudden visual and aural stimuli were noted in a number of cases. There was an acute hallucinatory delirium in a child of ten years suffering from hysteria which lasted from one-half to two hours and was the result of a sexual trauma at the age of seven years. A child who repeatedly ran away from home was severely punished by the mother and gradually developed an atasia-abasia. In this case the act of running away was based on a feeling of compulsion to do so. Compulsory ideas and phobias of various kinds were elicited from children six and seven years old. Idiosyncrasies which had their origin in superstition, and strong aversion for certain foods based upon an unpleasant personal experience were met with repeatedly. The suggestion of a resemblance between one child and an insane aunt caused the patient to be ob-

1. Handbuch der Nervenkrankheiten im Kindesalter. Berlin. 1912.

sessed with the idea that she would be insane at the age of twenty-five, the exact age of the aunt.

These few examples illustrate the influence of personality, environment and careless suggestion in the development of hysteria in childhood. Out of two hundred cases of hysteria in the adult I was able to collect one hundred and seventy-three cases that had their origin in a psychic trauma occurring between the ages of four and ten years. In ninety per cent. of the cases I was able to show a neuropathic disposition in one or both parents. In two hundred cases of adult neurasthenia between the ages of eighteen and forty-five years, there were but twelve per cent that gave a history of nervousness in childhood. In forty-two per cent. of all cases I was able to trace a neuropathic disposition in one or both parents. In all of the twelve per cent there was a history of nervousness in the parents.

CONCLUSIONS.

The conclusions one may draw from the analysis of the two hundred cases of nervous children are, that neurasthenia, pure and simple, is not frequent in the earlier periods of childhood. It is not as a rule hereditary and neurasthenia of adult life is not a persistence of childhood neurasthenia. The most common causative factor in childhood is mental overwork without the requisite periods of rest owing to the patient's surroundings.

In cases of endogenous uncomplicated nervousness, a marked neuropathic disposition is prevalent and no doubt is the hereditarily weak child which has diminished resistance and is unable to cope with the more strenuous mental life. This form is not observed until the school age is reached and continues in adult life to form the group known as nervous men and women, and possibly may also include the cases grouped under psychasthenia. Complicated endogenous nervousness is observed much earlier in the child, the youngest in the series being one year old. It is the most frequent form of nervousness in childhood and shows the importance of physical disease in the production of nervous disorders.

Hysteria in the adult is a persistence of the disease in childhood in the majority of cases. The disease itself is not hereditary but may to a certain extent be dependent upon a predisposition, either acquired or hereditary.

DISCUSSION.

DR. C. D. CAMP: I have been very much interested in Dr. Klingmann's paper, although I must confess that I am interested in the subject somewhat as an amateur. It is my impression that we should make a careful distinction between nervous diseases in children and "nervousness in childhood." My experience has been that nervous diseases in childhood present about the same problems as do nervous diseases in adults. We have all of the organic diseases in childhood that we have in adults, or practically all. We have cases of paresis, for instance, which are practically the same as paresis in the adult, and we certainly have cases of hysteria and neurasthenia in childhood which differ very little from those diseases in adults. On the other hand, "nervousness in childhood" has always seemed to me to be due to some condition outside the nervous system. Whenever I see simply a nervous child, an irritable, restless, disobedient child, I consider it certain that there is some cause outside the nervous system; some trouble with the eyes or the teeth, the nose and throat, or some other part of the body.

DR. D. M. COWIE: I am very glad to have listened to Dr. Klingmann's paper. The subject of course, is of very great interest to all physicians, particularly those who are engaged in general practice. My personal opinion about the cause of the numerous manifestations of nervousness in children is that they are due in a great part to environment. Attention has been called to what I believe to be a very pernicious habit, that of amusing children. Children should not be brought up with the idea that they must be amused all the time. It is surprising how little care normal infants and children require in order to keep them happy. If they are kept clean, warm, dry and properly fed, they will amuse themselves with very few playthings. A child should be allowed to grow like a plant. All it needs is a little cultivation. When it reaches the age of six months it will sit up and will insist on doing so if it is a normal baby. When it is a year old it will make efforts at locomotion, all without any help. The child has an equal capacity to amuse itself. The infant should be allowed to develop itself. Leaving a baby or an older child entirely to its own devices on the other hand is equally pernicious in its effects. Extremes must be avoided. It is wrong to let a child lie all day in the same bed. Infants treated in this way frequently make slow development and do not manifest the same intelligence that children do who are taken up occasionally and moved from one part of the house to another, and thus given a change of position as well as of scene.

THE INJECTION OF ALCOHOL INTO THE GASSERIAN GANGLION IN THE TREATMENT OF TRIFACIAL NEURALGIA.

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The most scientific as well as the most satisfactory treatment for trifacial neuralgia is the removal of the cause. In 1909, I published a paper (The Cause and Treatment of the Trifacial Neuralgia[1]) in which I dwelt at length on this point. In some cases, in spite of diligent search the cause is undiscovered; these are usually in patients well advanced in years and it is to the treatment of this class of case that I would especially call attention. Electricity may be of some benefit to them, but I have never seen one cured that way. Medical

1. Physician and Surgeon, August, 1909.

treatment is not curative unless directed towards the cause—that is, quinine in malarial cases, iron in anemia, et cetera. The injection of alcohol, osmic acid or other substances into the nerve, either deeply or peripherally, is usually a measure affording temporary relief only; the nerve almost always regenerates and the pain returns. The removal of the Gasserian ganglion, surgically, is usually curative but the operation is a very difficult and dangerous one; the best surgeons often hesitate to attempt it and if the patient survives the operation there is great danger of trophic ulcer of the cornea and also danger of cerebral hernia.

It is generally conceded that, in order to prevent recurrence of pain, the ganglion must be destroyed and, in 1909, Harris suggested that this might be done by passing a needle through the foramen ovale and injecting alcohol into the ganglion. In 1912, he published three cases which he had treated this way, though Offerhouse and others had treated the suggestion as quite impossible. Hartel, in Germany, also injected the ganglion but with a somewhat different technic. Taptas, in France, used the same method as Harris.

I became interested at once on seeing the paper by Harris and, after some practice in the anatomical laboratory, injected my first case, April 19, 1912. The patient was fifty-six years old and had had neuralgia for fourteen years. He had been extensively treated and had an operation on the nerve with temporary relief. After the injection it was noted that there was analgesia in the distribution of all three branches of the nerve and he had no attacks. He was discharged from my service in the Hospital six days later and I have heard that his neuralgia is cured but have had no opportunity to re-examine him.

The second patient was a woman, age forty-six, with severe trifacial neuralgia of two years' duration. She was admitted to the Hospital in December, 1912, and on January 6, 1913, had an injection of alcohol into the peripheral nerves at their exit points on the face, with complete relief. On Feb. 17, the patient came back to the Hospital, the pain having returned two days before. The Gasserian ganglion was injected, Harris method, on February 24, 1913. In less than ten minutes after the injection there was complete analgesia of the right side of the face in the distribution of all three branches of the fifth nerve, and the right side of the tongue. The corneal reflex was lost on that side. Sensation to pressure was preserved. On February 27, it was noted that she had a vesicular eruption about the right corner of the mouth resembling herpes zoster. On March 2, she had no pain and the area of analgesia was the same as before. A steel pin was thrust through the right side of the tongue without causing pain, though the patient said that she felt it going through. The corneal reflex was lost but there was no keratitis. An examination made December 11, 1913, showed the area of analgesia slightly less extensive but otherwise the same as at the previous examinations.

The third patient was a farmer, aged sixty-eight years, with typical and very severe neuralgia in the left side of the face, duration four years. His blood pressure was 200 mm. Hg. but, except for the manifestation of the neuralgia, his neurologic and physic examination was negative. He was given an injection of 1 c.c. of 1 per cent cocaine in 80 per cent alcohol into the Gasserian ganglion, July 24, 1913. Analgesia of the left side of the face was complete inside of a few minutes. After the withdrawal of the needle he said that he felt dizzy and nauseated and there was noticed a weakness in the muscles of expression on the left side of the face and a paralysis of the left external rectus muscle but this paralysis was transient and there was no trace of it the following day. There remained a permanent analgesia of the left half of the face in the distribution of the fifth cranial nerve (Figure 1),

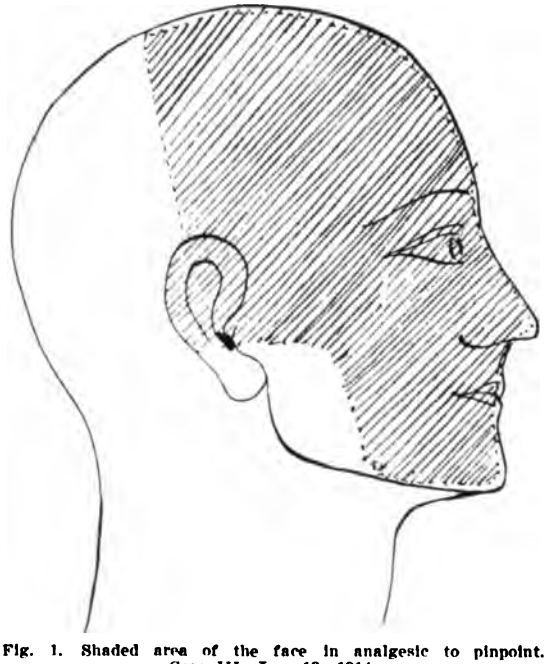

Fig. 1. Shaded area of the face in analgesic to pinpoint. Case III, Jan. 13, 1914.

also analgesia of the left half of the tongue, and of the mouth as far back as the middle of the tonsil. The left cornea was anesthetic and the reflex abolished. It was also noted that the temporal and masseter muscles on the left side did not contract on mastication. Some interesting physiologic studies have been made on this patient relative to the functions

of the Gasserian ganglion. Dr. Canfield reported that the tympanic membrane was anesthetic, the only response to the probe being a ringing tinnitis.

The patient's present condition can be shown you, for he has very kindly returned to the Hospital at my request for re-examiation. He has had no pain since the injection and feels very well. The extent of the analgesic area is about the same as on previous examinations and the corneal reflex is still absent. There is no sign of keratitis.

Using aseptic precautions the needle is inserted through the skin opposite the lowest part of the sigmoid notch and pushed upward and backward to the foramen ovale; after recognizing this point the needle is pushed not over one centimeter through the foramen and the alcohol injected. (Figure 2.) The position of the needle is shown in the illustration. (Figure 3.) The appearance of the analgesia in the forehead is an indication that the ganglion has been reached for the ophthalmic division of the fifth, of which the supraorbital is a branch, passes directly into the orbit and the alcohol would not influence it unless the needle had passed through the foramen ovale.

The insertion of the needle is not without some danger for important structures are very close; the middle meningeal artery, passing through the foramen spinosum, the cavernous sinus, et cetera, and injury to them would probably have serious consequences but no case has yet been recorded in which there has been a serious accident when using the Harris technic.

I feel safe in saying that the demonstrated possibility of destroying the ganglion by simply injecting alcohol into it, without opening the skull, is a great step forward in the treatment of intractable cases of tic douloureux but it should only be done after every effort to find or remove the cause has failed and the peripheral injections or operations do not give relief.

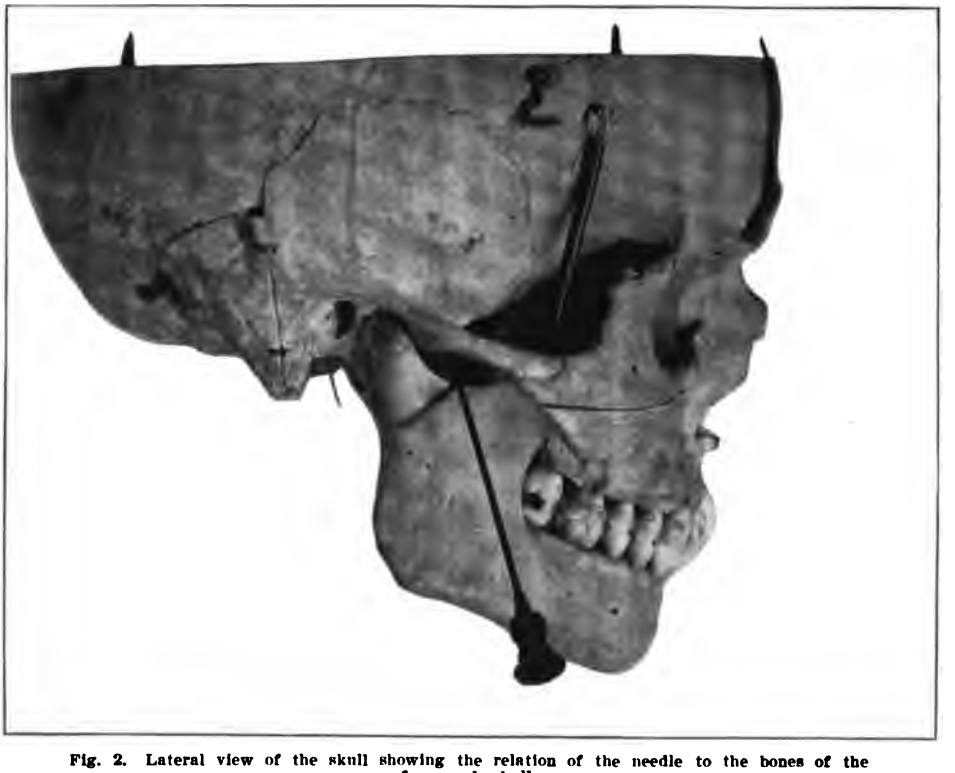

Fig. 2. Lateral view of the skull showing the relation of the needle to the bones of the face and skull.

Discussion

Dr. C. G. de Nancrede: I agree entirely with Dr. Camp concerning the seriousness and difficulty attending the Hartley-Krause operation. I need not dilate further upon the dangers of this method which sometimes necessitates operating in two or three stages because of the free hemorrhage which obscures the field of operation, and is sometimes dangerous to life. The anatomic differences in this particular part of the cranial vault are liable to relatively great variability, and I do not see how in certain cases one can surely avoid injuring large bloodvessels. Sooner or later, those who employ this method will surely meet with such accidents. I think that it is far better before undertaking the injection or excision of the ganglion, to employ more conservative measures such as the injection or

removal of the peripheral branches. I have frequently seen bad cases of trifacial neuralgia given very prompt relief, for relatively long periods, from conservative methods such as these. I do not think Dr. Camp has done justice to the efficiency of these methods. Furthermore, a change in climate will often effect a distinct relief where advanced arteriosclerosis is present avoiding marked changes in atmospheric pressure which causes circulatory changes in the ganglion or its branches. I think that all the conservative and less radical methods should be tried before considering either injection or removal of the ganglion.

I do not say Dr. Camp's operation is impossible, for he has succeeded, and I recently referred a private case to him for this operation, but I do say that I am perfectly sure if injection operations be tried often enough, serious accidents will occur.

Dr. R. Bishop Canfield: I can vouch for the success of Dr. Camp's injection in the cases I have seen. I would not like to turn over to him my cases of internal pressure, but given a case where there is no question of peripheral irritation, I can see a distinct place for the injection of the ganglion. Certainly the cases I have seen of his have been perfect in their results and with no ill effect so far as I could see. I agree with Dr. de Nancrède that it is better to have the peripheral causes removed first, but I should certainly prefer having my ganglion injected to having it removed.

Dr. Camp (closing the discussion): I have been very much interested in Dr. de Nancrede's experiences. As I said at the beginning of my paper, it is certainly more scientific to remove the cause, if it can be found. As a matter of fact, it is remarkable how many cases one can cure that way if one is sufficiently patient and diligent. I have had about forty cases of trifacial neuralgia in the past two years and only three have needed this injection. Dr. de Nancrède has had to operate on the Gasserian ganglion and has made a strong showing as to the dangers and difficulties involved in this operation. It is true that one would prefer to do peripheral injections but recurrences are frequent. One of the patients reported this evening had had several peripheral injections and two peripheral operations in which a large part of the superior maxillary had been cut away, and then there was a recurrence.

Fig. 3. View of the base of the skull from above.
The needle is in about the position of the Gasserian ganglion.

(1) A CASE OF OBSTRUCTION OF THE CENTRAL RETINAL VEIN.

(2) A CASE OF OBSTRUCTION OF THE OPHTHALMIC VEIN.

(3) A CASE OF HEMORRHAGE AT THE BASE OF THE BRAIN WITH PRESSURE SYMPTOMS RESULTING IN IMPEDED VENOUS FLOW, PARALYSIS OF EXTRINSIC MUSCLES AND PARTIAL DEAFNESS.

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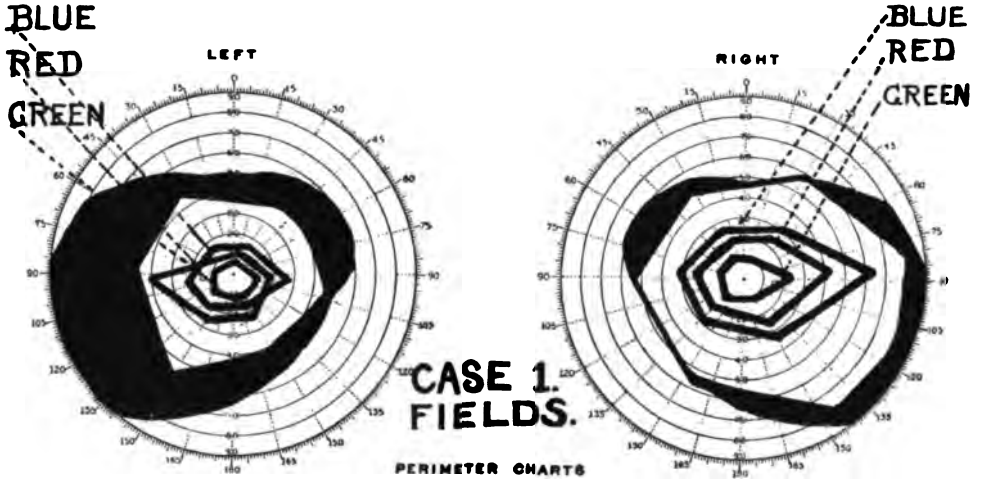
CASE I. A case of obstruction of the central retinal vein, possibly due to proliferation of the intima.



C. P. male, aged 38, American, farmer. Entered the Clinic of Ophthalmic Surgery December 15, 1913, complaining of dimness of vision in the left eye.

History: Four weeks ago the patient first noticed that his vision in the left eye was blurred. This dimness progressed for two weeks, but has remained stationary since that time. Vision is more blurred temporally and objects seen have a reddish color.

Examination—Vision right eye 5/4, left eye 5/20. Lids, conjunctiva and external appearance of eyeball normal. No proptosis as shown by the measurements taken with the exophthalmometer. Tension, right eye, 30 mm. Hg., left eye 23 mm. Pupillary reflexes normal.

Ophthalmoscopic Examination—Right eye. Vessels of the retina show slight arteriovenous compression, beginning corkscrew veins, retina slightly edematous. Fundus otherwise negative.

Left eye. Media clear, disc edematous, blurred and slightly swollen. Veins markedly engorged, irregularly distended, most marked in the superior temporal portion. Retina mottled throughout by diffuse, striated and radiating hemorrhages (nerve fiber layer), the whole retina edematous, in places completely obscuring the veins. Center of the fovea yellowish, hemorrhages darker in color radiate from the center of the fovea.

Fields—Right eye. Very slight contraction for form and color. Left eye. Form field contracted, except nasally, temporal field narrowed to 50°, color field for blue and red concentrically contracted and confused; red slightly less proportionately contracted.

Orientation. Excursion normal, both eyes.

Blood examination—B.P. 110, Hemoglobin 95%, R. B. C. 4,980,000. W.B.C. 6550.

Lymphocytes, small 32%, large	4%
Polynuclears, neutral	60%
Polynuclears, eosin	3%
Transitional	1%

No other forms seen in count of 250 cells.

X-Ray Report—Plates negative, except for slight shadow just to the left of vertix at termination of middle meningeal artery.

Otolaryngologic report negative. Wassermann report negative. Medical report, pulminary emphysema, urine negative, blood pressure normal. Tuberculin reaction negative.

This case presents a negative history, except for loss of vision coming on gradually. Ophthalmoscopic examination revealed a typical picture of obstruction of the central retinal vein.

A thrombosis in the central vein or in its branches causes ophthalmoscopic appearances which were formerly credited to embolism of the central artery or to hemorrhagic retinitis.

The pathologic aspects of venous thrombosis have been admirably investigated by Coats. Clinically when one sees large hemorrhages and enormously swollen and tortuous veins partly buried in retinal edema, obstructions to venous return flow must be considered. When these changes are limited to one eye, and there is no exophthalmos or other evidence of obstruction of the ophthalmic vein, the conclusion seems inevitable that the obstruction must be in the central vein and not farther back.

There may be signs of widespread vascular disease in the form of thickened peripheral vessels and cardiac hypertrophy, or, of nephritis.

Pathologic examination of a large number of cases has shown that the obstruction may be due to a thrombosis, to a proliferation of the intima, or to a combination of these conditions The loss of vision is more sudden in cases of thrombosis and there are no prodromal symptoms.

According to Parsons the different pathologic changes which have been put forward in explanation of the clinical picture of thrombosis of the central vein are as follows:

1. Thrombosis in the central vein. 2. Occlusion of the central vein by proliferation of the intima, but without thrombosis. 3. Multiple thrombi in the retinal veins, but without a thrombus in the central vein. 4. Multiple emboli or perhaps thrombi in the retinal arteries. 5. Changes in the retinal vessels, (degenerative). 6. Hemorrhage into the substance of the optic nerve.

Several cases are recorded in which on pathologic examination no thrombosis nor other impediments were found in the veins. Usually the thrombus or other obstruction is situated either at the lamina cribrosa, or a short distance behind it, more rarely at the point where the central vein makes its exit from the nerve.

These cases of thrombosis of the central retinal vein are prone to be followed by glaucoma, and as it is for the relief of this complication that enucleation becomes necessary, it is sometimes difficult or impossible to differentiate between the primary and secondary pathologic changes.

Frequency—Thrombosis occurs about once in three thousand ophthalmic cases and most frequently in persons accustomed to much toil, and especially to much stooping. Of the 20 cases reported by Ammann, 13 occurred in farmers who did gardening, and 2 others in smiths. Nearly all of the cases reported occurred between the ages of 40 and 80. Men were more often affected than women. Most of the cases showed marked angiosclerosis.

Diagnosis—The gradual loss of vision, in the case here reported, together with the absence of all symptoms suggesting the source of a thrombus, leads to the diagnosis of obstruction of the central vein, due to proliferation of the intima.

Prognosis—In favorable cases the hemorrhage disappears by absorption and useful vision may be retained. In the majority of cases, however, the vision is lost. A few develop glaucoma and the eye is lost.

Treatment is unsatisfactory.

CASE II. A Case of Obstruction of the Ophthalmic Vein due to pistol shot wound.

S. C., male, aged 22, English, cook, entered the Clinic of the Ophthalmic Surgery December 15, 1913, complaining of diplopia, exophthalmos of the left eye, and difficulty in walking.

Photograph of Case II.
A case of obstruction of the opthalmic vein.

History—Four months ago the patient was shot in the mouth with a thirty-two caliber revolver. Two attempts were made to remove the bullet. Immediately following the accident the pain was severe in the head, most marked at the vortex. About two weeks later, he began to have pain over the left eye accompanied by nausea and vomiting. The attacks came on as often as four or five times daily. They continued several days, then gradually grew less in severity and frequency. The patient now suffers no attacks of nausea or vertigo, but has occasional pain along the course of the left supraorbital vein. Diplopia was first noticed after the operation, but disappeared in four days, to return again three or four days later, and has remained constant since that time.

Examination—Vision right eye 5/4, left eye 5/4.

External examination. Right eye, negative, left eye, eyelids swollen, conjunctiva of lids normal, ocular conjunctiva congested, especially in the palpebral fissure.

Eyeball, marked proptosis, eye easily moved in all directions, and exophthalmos diminished by pressure. Measurement with exophthalmometer, left eye 7 mm. more forward than right eye. Tension with tonometer, right eye 20 mm. Hg., left eye 30 mm. Hg. Pupillary reflexes normal, pupil oval, long axis up and in.

Ophthalmoscopic Examination.—Right eye, normal. Left eye, Media clear, nerve head congested, edges blurred, deep physiologic cup, lamina cribrosa seen, whole retina engorged,

especially the inferior temporal vein, whole retina edematous.

Fields—Form field of the left eye, slightly smaller than that of the right. All the color fields are somewhat contracted, no dyschromatopsia or other abnormality.

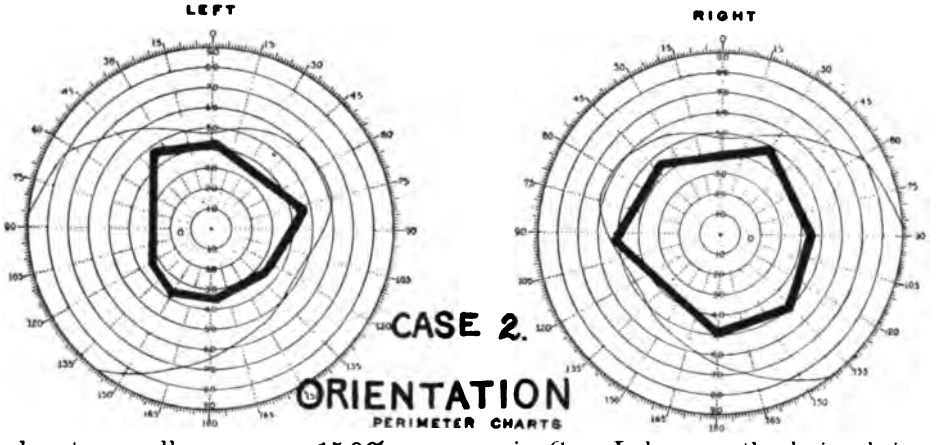
Fields of Fixation—Although the excursions appeared nearly normal, the fields of fixation show a slight limitation of the movement in temporal fields, more marked in left eye.

Blood Examination—B.P. 110 mm. Hg. Hemoglobin, 90%. R.B.C. 5,400,000; W.B.C., 10,450; Myelocytes, 0; Normoblasts, 0; Megaloblasts, 0.

Thrombosis of the ophthalmic vein is accompanied by pain over the brow, along the course of the supraorbital vein, marked chemosis of the conjunctiva, with absence of the subconjunctival hemorrhages, proptosis (non-pulsating and partially reducible by pressure), diplopia which may be accompanied by vertigo, nausea and vomiting. Ophthalmoscopic examination reveals veins moderately engorged, nerve and retina edematous.

As the course of the bullet was along the floor of the orbit, the pressure on the vein must have been due to fracture with displacement of bone in the orbit.

The changes in the fundus are not so marked



Lymphocytes, small	15.8%
Large	1.5%
Transitionals	4.4%
Polynuclear Neutral	75.9%
Polynuclears Eosin	1.6%
Mast cells	.7%

X-Ray Examination—There is a foreign body apparently in the petrous portion of the temporal bone. It lies about on a line connecting the two external auditory meati and possibly slightly in advance and a trifle below. Its upper margin is tangent with the lower margin of the left external auditory canal and about one-third of the distance from the sagittal plane to the auricle. No fracture lines can be discovered. Skull is otherwise negative.

Otolaryngologic Report—Bullet wound in left soft palate; powder marks.

Nose: Very badly deviated septum with small shelving spur on floor making contact.

Ears: Show no result of injury. Patient has spontaneous nystagmus of horizontal and rotary character.

Apparently both cochlea and vestibule of the left ear are quite destroyed. .

Hearing in right ear, whisper 21 ft.

1-12-14. Vertigo test is diminished.

Hearing: Whisper in right ear normal; in left ear whisper test one inch, voice 12 to 18 inches.

as in Case I, because the lesion being farther back, allows the collateral circulation to become established, the communication between the orbital and facial veins being very free.

Case III. A case of hemorrhage at the base with pressure on sinus, deafness on left side, paralysis of the extrinsic muscles, nystagmus, and disturbance of return venous flow as shown by swelling of lids, marked chemosis of conjunctiva, engorgement of the retinal veins and protrusion of the eyeball.

Photograph of Case III.
A case of hemorrhage at the base of brain with pressure symptoms.

A. B., aged 20, American, occupation farmer, entered the clinic of Ophthalmic Surgery November 3, 1913. The patient was referred by Dr. M. S. Gregory, Eureka, Mich.

History—Eight weeks ago the patient fell from a bicycle severely bruising and scratching the right side of his face and head. There was some contusion of the right orbital region, although the eyes were not injured.

Four weeks ago the patient began to have pain in the left eye, which extended from the region of the eye to the top of the head. This was followed by photophobia, lacrymation, and gradual failure of vision. The eyeball became red and the lids swollen. Within a week the eye began to protrude and the patient suffered from headache, nausea and vomiting. He feels fairly well when not nauseated and when the headache is not severe; his appetite is good. Diplopia at first was denied, but afterwards admitted.

Examination—Vision, right eye 5/5, left eye, 5/30. Marked scarring, fine linear parallel lines, along right side of the face.

External Examination—Right eye. Palpebral aperture widened, lids slightly retracted. Eye cannot abduct beyond the median line, elevation and depression about normal, abduction slightly limited. Iris reflexes normal. Left eye, marked exophthalmos. Partial ptosis, upper lid; cornea 1/2 covered. Eyelids cannot be closed because of chemotic swelling of the conjunctiva. Eyelids not thickened, some dilation of veins with edema of lid margins, upper lid freely movable, very slight discharge of a faint amber tint. The conjunctiva of the upper lid is congested. Ocular conjunctiva. Upper half-veins prominent, distended and twisted from limbus to fornix, no especial ciliary injection, as such. Lower half swollen, chemotic, opaque, protrudes between lids so eye cannot be closed. Position of the upper lid limits the conjunctival swelling so the border is nearly horizontal. Corneal surface slightly stippled. Iris congested but no marked iritis. Pupils freely movable. Reflexes normal. Exophthalmometer shows left eye protruding 19 m.m. being 7 m.m. further forward than right eye. Excursions limited. The eye is convergent about 20°. Tension normal.

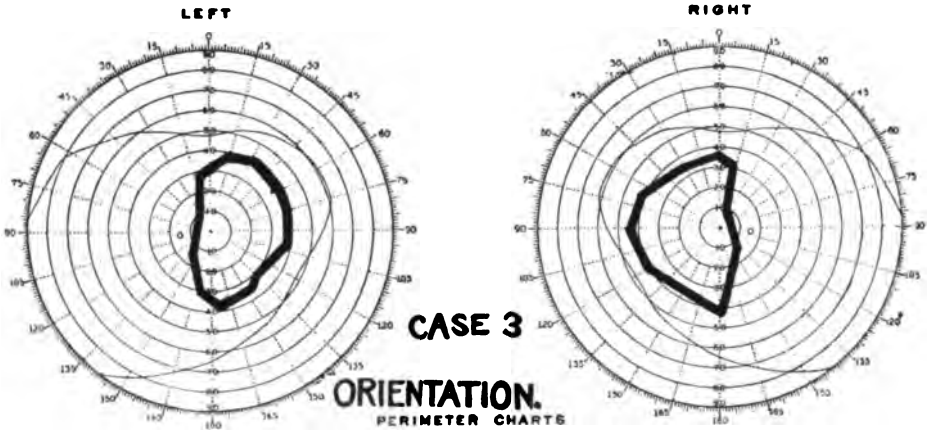
Ophthalmoscopic Examination—Right eye Disc slightly blurred and hyperemic otherwise practically normal. Vessels not tortuous, slight arteriovenous compression, otherwise normal Retina and choroid normal, macula practically normal, possibly slight edema.

Left eye. Disc rings visible, but blurred so that disc borders are quite indefinite. Slight exudate overlying lower nasal border of disc. Veins markedly engorged and tortuous, arteries normal. Distinct arteriovenous compression. Retina hyperemic, edema marked; retina down and temporarily swollen and infiltrated. Macula markedly edematous, foveal reflex lost. No hemorrhages present in fundus. With fingers, slight pulsation of orbital contents, which could also be seen on close observation, probably transmitted.

Treatment—Protective pressure bandage applied and patient kept as quiet as possible. Atropin to keep pupil moderately dilated.

11/28. Fields. Right, normal. Left, slight contraction of form and color fields.

Orientation fields. Right, normal nasally, very markedly limited temporally. Left, markedly limited temporally, less nasally, slightly limited below.



Doplopia chart. Marked homonymous diplopia, varying but little in all nine positions.

Blood and urinary examination negative.

X-Ray Examination, negative.

Otolaryngologic Report. Spontaneous nystagmus of intracranial character. Hearing test, whisper in both ears.

Neurologic Report. Paralysis of external rectus, both sides. Some nystagmus on rotating right eye to the left; otherwise negative.

Wassermann Report. Negative.

Subsequent History—At no time has there been an increase in temperature or change in the blood.

11/13. Slight improvement. Less pain in eyes and head.

11/21. Eye can now be nearly closed, movements better, conjunctival swelling much reduced. Patient more comfortable.

11/28. Exophthalmos reduced to 3 mm. Vision, right eye 5/5; left eye, 5/30.

12/1. Ophthalmoscopic Examination. Disc swollen 1 diopter; retina more opaque, rendered hazy by diffuse exudate, edema more marked. There are now many minute circumscribed hemorrhages temporally mostly small and rounded; some large and more diffuse.

12/10. Chemosis of the eyeball has disappeared and tortuosity of vessels now quite as marked below as above. Fundus the same. Exophthalmos 4 mm.

This case presents a non-pulsating monocular exophthalmos with marked chemosis of the conjunctiva, engorgement of retinal veins, edema of the retina with hemorrhages, together with diminished hearing on the same side, nystagmus of intracranial type, and paralysis of both external recti. There are no evidences of infection or inflammation as shown by the absence of fever and blood changes.

DIAGNOSIS

Tumors of the orbit either primary or secondary to sinus involvement can be excluded by the mobility of the globe in all directions and partial disappearance of exophthalmos on pressure. The vascular tumors, aneurism or aneurismal varix, may be eliminated by the absence of distinct pulsation or a bruit. Thrombosis of the ophthalmic vein could give all the symptoms referable to the eye, but could not account for the loss of hearing, paralysis of the external recti, nor the presence of the nystagmus. Thrombosis of the cavernous sinus might give the eye symptoms here present, but all the nerves which traverse the sinus are liable to injury, the third being nearly always affected. Again in cases of cavernous sinus thrombosis, through the medium of the circular sinus, the process may extend to the other side, a complication which occurs in more than 50 per cent. of the cases (McEwen). Then, through stasis in the emissary vein of Santorini, edema over the mastoid may occur if the lesion originates in the sinus.

The history of traumatism followed by the symptoms as given, together with the marked improvement observed since the patient came under observation, seems to justify the diagnosis of hemorrhage, leading to pressure symptoms. The cause of the double abducens paralysis is difficult to explain.

DISCUSSION.

Dr. Geo. Slocum: These cases are indeed exceedingly interesting, more especially, by reason of the difficulty in the diagnosis of the cases presenting exophthalmos, and because of the points of similarity of the vascular fundus lesions, all of which are due to interference with the venous return flow. In the cases with exophthalmos one must differentiate between cavernous sinus thrombosis and venous compression or obstruction resulting from the trauma. In cavernous sinus thrombosis there is often pronounced exophthalmos with venous obstructions. However, in cavernous sinus thrombosis, pronounced and severe symptoms of sepsis are present. These cases do not present such symptoms and the blood examination is negative. Two-thirds of the cases of cavernous sinus thrombosis depend upon disease of the middle ear, and septic sinus thrombosis is always fatal unless surgical interference is successful. We have no ear disease in these cases. Marasmic sinus thrombosis is not always fatal but this form occurs only in the two extremes of life.

In the second case presented there must have been some fracture of the bone where the bullet passed through the base of the skull, but X-ray examination failed to reveal its location. A fracture might have occurred at the base, in the neighborhood of the sella turcica, causing a displacement of a fragment of bone, which could produce a compression of the anterior end of the cavernous sinus, sufficient to impede the return flow from the ophthalmic vein. Lack of the usual anastomotic connections of the ophthalmic vein would then result in pronounced exophthalmos with diplopia, from a simultaneous compression of some of the nerves of the eye muscles, all of which pass through, or in the walls of the cavernous sinus.

In the case of the patient who was thrown from a bicycle, no fracture was discovered by the X-Ray however, a fracture of the body of the sphenoid at the side of the sella turcica, too small to be revealed by the plate, might easily produce a hemorrhage from the vessels of the diploe, which could compress the sinus from below where the sinus wall is very thin, sufficiently, to obstruct the return flow from the ophthalmic vein and thus produce the symptoms. This would answer all the questions presented in the diagnostic study, with the exception of the bilateral abducens paralysis in the last case. Whether the hemorrhage came from such a fracture of the sphenoid or whether it came from the rupture of one of the blood vessels in the immediate neighborhood of the cavernous sinus is a question for consideration but when we remember the dense fibrous character of the upper wall of the sinus and the fact that the sinus is thereby held firmly open, even when empty of blood, the probability of a hemorrhage on the upper surface of the cavernous sinus producing pressure, appears remote. It would therefore seem more than probable that the hemorrhage occurred from the under surface of the cavernous sinus, that is, from broken veins in the diploe. The possibility, that a fragment of bone from such a fracture might take part in a compression of the sinus in this case also, must be considered.

Dr. Parker (closing the discussion): There is one condition in the last case reported that does not seem to be fully explained, namely, the paralysis of the external rectus in each eye. The absence of diplopia would suggest the possibility of the existence of a lesion of long standing, independent of his accident. Patients who develop a sudden paralysis of the ocular muscles usually complain of the double vision as the most distressing symptom, while this patient suffered little or no discomfort from this symptom. A fracture of the sella turcica might lead to pressure on the sixth nerve on both sides, while the resulting hemorrhage might be limited to the left side. It would not be difficult to imagine a fracture at this point which might not be demonstrable by the X-ray. These are rare cases, and to have all three under observation at one time is most unusual.

(1) A CASE OF HYDRAMNIOS AND TWIN PREGNANCY.

(2) A CASE OF ABDOMINAL CESAREAN SECTION FOR AN OBLIQUELY CONTRACTED PELVIS.

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I have for your consideration this evening two obstetric cases showing features of interest.

CASE 1. Mrs. W., age 28, entered the Maternity Clinic November 8, 1913, complaining of dyspnea, great abdominal distention, inability to retain food by mouth and difficult urination. Her history was negative until the present pregnancy. She had had five children, all living, without complication during the pregnancies and puerperia, and one abortion at two and one-half months, cause unknown. From her history, she was six months pregnant. The present pregnancy had been in all respects uneventful until the fifth month, four weeks before entering the Hospital. At this time she first began to notice a rapid abdominal distention, accompanied by difficult respiration. In three weeks the waist line increased slightly more than six inches. For several days prior to coming to the Hospital she had been unable to lie down, or to retain food and urination had become difficult. Quickening was first noticed at the beginning of the fifth month, and movements had been felt daily since.

Examination: General: Patient of moderate build, good nutrition, pulse 118, respiration 26, temperature 98.6°. Conjunctivae and mucous membranes of good color. Face flushed and anxious, dyspnea marked, slight cyanosis of lips.

Thorax: Lungs negative. Heart displaced outward and upward. Breasts: pendulous, Montgomery's follicles enlarged, primary and secondary areola present. Colostrum easily expressed.

Abdomen: Markedly distended from pubes to ensiform, symmetrical, domeshaped, much larger than full term pregnancy. Slight bulging in flanks. (Figure 1.) Broad striae in lower quadrants. Linea nigra to umbilicus. Palpation gave very cystic feel, some edema above symphysis. No tumor mass felt. Fetal parts not made out. No movable areas of dullness. Auscultation showed a faint fetal heart in the left lower quadrant half way on a line between umbilicus and anterior superior spine, rate thirty-six to quarter minute. A second fetal heart could not be heard, although the possibility of twin pregnancy was thought of. There was marked edema of the feet and abdominal wall above symphysis.

Vaginal Examination: External and internal perineum lacerated. Marked Chadwick's sign. Moderate whitish vaginal discharge. Cervix: old bilateral laceration, soft and patulous. Admits finger with ease. A fetal head at superior strait, freely movable.

Diagnosis: From the above findings, combined with the history of rapid distention, a diagnosis of hydramnios was made.

Treatment: As it was obvious that the patient could not continue throughout pregnancy in her present condition on account of the daily increasing distention and inability to eat or sleep, it was decided to puncture the membranes through the cervix for immediate

Fig. 1. A case of hydramnios with twin pregnancy.

relief. The patient was accordingly prepared for operation and put upon the table, but was unable to lie flat on account of the dyspnea and had to be supported. The membranes were punctured with a fine trocar as high up as possible and four liters of amniotic fluid drained off with immediate relief to the patient who fell asleep for the first time in several days.

The patient was immediately put to bed in the hope that with the high puncture of the membranes only a portion of the amniotic fluid would come away. However, the fluid continued to drain and three or four liters came away in the bed, making in all between seven and eight liters. The uterus was mas-

saged to facilitate contraction and the patient left in good condition. About six hours later, the patient went into labor and was delivered of still born, premature double ovum male twins. The puerperium was uneventful and the patient left the hospital on the thirteenth day in excellent condition. The Wassermann reaction was negative.

Hydramnios occurs about once in two hundred pregnancies. Minor degrees with two or three liters of amniotic fluid are not uncommon, but the more marked grades are not frequent. In rare instances the uterus may contain an almost incredible amount of fluid, Küstner having observed fifteen liters at the fifth month, and Schneider thirty liters at the sixth month.

There has not as yet been a satisfactory or universally accepted idea as to the etiology of hydramnios. From the fact that the amniotic fluid is normally derived from the fluids of the mother which have been modified by the secretory activity of the amniotic epithelium, while the fetal kidneys take no part in its production, except in abnormal cases, it is impossible to give an explanation for its excessive production which will be applicable to all cases. Generally, however, authorities agree that the excess of amniotic fluid may be derived from several sources: from the fetus, from the mother, from the mother and fetus and occasionally from the amnion. According to Williams, "in something less than one-half the cases careful examination of the fetus after death reveals some abnormality which may or may not bear a causal relation to the disease. Most frequently the abnormality which is supposed to give rise to hydramnios is to be found in lesions which cause obstruction to the circulation, either in the cord or within the foetus." Opitz observed scirrhotic changes in the liver in all his cases. Woerz and Bar, and Nuberding found heart disease. Many authorities believe hydramnios to be due to an excessive urinary secretion. In Wilson's analysis of fifty-one cases of hydramnios occurring in multiple pregnancy, twenty-two of the twins were uniovular and when we take into consideration that these are much less frequently observed than the double ovum variety it becomes evident that something connected with the former has a bearing on the excessive production of amniotic fluid. As a rule, the hydramnios is limited to a single amnion. The kidneys and heart of the fetus having hydramnios are both actually and relatively larger than those of the other twin. At times cardiac and renal disease or visceral syphilis in the mother are associated with edema of the placenta and an increased transudate into the amnion. Wolf has shown that nephrectomy in pregnant rabbits is followed by increased renal activity on the part of the fetus, with consequent hydramnios. Occasionally inflammation of the amnion itself is supposed to favor the production of the condition.

In the case under consideration it was at first thought that the twins were uniovular because of the firm fusing of the placentae. On more minute examination, however, two separate placentae could be distinguished although they could not be separated. The membranes were rather badly torn but the remnants of two chorions could be found. This was proof that the twins were of the double ovum variety. At autopsy the larger twin weighed 1080 grams, the smaller 730 grams. According to the pathologist, Dr. Warthin, the fetal heart of the larger twin was larger than normal for the size of the fetus, while that of the smaller was subnormal for its size. In the light of these findings the fact that the twins were double ovum can be explained only in one way; that contrary to the rule in double ovum twins the blood spaces of the two placentae had fused as well as the surrounding tissue and that to all intents and purposes they were single ovum twins in which the stronger heart had dominated the circulation and enlarged at the expense of the weaker.

CONTRACTED PELVIS, CESAREAN SECTION.

CASE II. M. S., age 23, primipara, entered the Maternity Service September 24, 1913. Her family history is negative. Her personal history shows one incident bearing on the case. At the age of two and one-half years the patient fell, severely injuring the right hip. After this accident she was in bed for a year and did not walk again for eighteen months, and then with a limp which has persisted. There are no points of interest in the history of the present pregnancy which was in all respects normal. The Wassermann reaction was negative. The following are the points of interest in the physical examination:

Abdomen: Domeshaped, many fresh striae in lower quadrant, faint linea nigra to umbilicus Fundus at time of first examination, two finger breadths above the umbilicus. Fatal breech in fundus, back on right, small parts on the left. Fetal heart best heard in right lower quadrant, one-third the distance on a line from umbilicus to anterior superior spine. Position, right occipito-anterior.

The right leg is ten centimeters shorter than the left, and is fixed at hip. The pelvis tilts forward and the patient has a marked lordosis. (Figure 2). With the patient on her back the lumbar region cannot be brought closer than seven or eight centimeters to the table. The left anterior superior spine is two centimeters higher than the right.

PELVIMETRY:

Intercristal	25 cm.
Interspinous	25.5 cm.
Bitrochanteric	29.5 cm.
External conjugate	16.5 cm.
Pubic angle	85°
Bis-ischial	8 cm.
Antero-posterior of outlet	11 cm.
Anterior sagittal	5 cm.
Posterior sagittal	8¼ cm.
Diagonal conjugate	11 cm.
Conjugate vera	8.5 to 9 cm.

Fig. 2. Obliquely contracted pelvis due to early injury of the right hip. Cesarean section at term.

The X-ray confirmed the diagnosis of right occipito-anterior position and showed that the pelvis was asymmetrical. The neck of the right femur had almost entirely disappeared from what was in all probability a tuberculous process dating from the patient's fall when two and one-half years of age.

The classification of the pelvis is interesting. In the first place the deformity is asymmetrical. From the extra weight on the sound or left leg and the shortening in the right, the left side of the pelvis is shoved upward and compressed anteroposteriorly, giving an obliquity to the superior strait. The compensatory lordosis throws the promontory forward and increases the angle of the pelvic inclination with, as a consequence, a shortening in the external diagonal and true conjugate, giving a flat pelvis. Ordinarily the small difference between the intercristal (25 cm.) and the interspinous (25 cm.) diameter would make us suspicious of a rachitic pelvis, but as the patient gives no history and had no other signs of the disease, this can be ruled out. The bis-ischial diameter of the outlet measures eight centimeters, which is just within the limit of the "funnel pelvis."

Taking into consideration the obliquity of the superior strait there is present an obliquely contracted, flat, funnel pelvis.

It is in these "border line" cases with the conjugate vera of 7.5 to 9 centimeters that the greatest difficulty is found in predicting the course of labor. In the case under consideration (conjugate vera 8.5- 8) with the position right occipito- anterior, it was thought that labor would probably be spontaneous as the bi-parietal diameter was in relation with the long right oblique and as the child was of moderate size. However, upon second examination it was found that the position had changed to left occipito-anterior, the bi-parietal diameter now corresponding to the short left oblique diameter. In the light of this change of position, it was decided that the outcome of labor would be doubtful, inasmuch as even if descent did occur all obstacles to labor might not be overcome, since in many cases the inward projection of the ischii leads to faulty rotation. In the interests of both mother and child, Cesarean section at term seemed the procedure of choice.

Operation: The patient went into labor November 23, 1913 and was allowed to proceed for four hours. Rectal examination then showed the head still movable at the superior strait, and the patient was taken to the operating room for Cesarean section. The classical conservative operation was performed by Dr. Peterson, the patient returning to bed with a pulse of 80. The child was a healthy male and required no resuscitation. The convalescence was in all respects uneventful, both mother and child leaving the Hospital on the twentieth day after operation.

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Discussion.

Dr. Reuben Peterson: Acute hydramnios is rather a rare disease of pregnancy and interesting, since its causes are rather obscure and it usually calls for active treatment if the patient is to obtain any relief. If my memory serves me correctly I have seen at least four cases of this complication. In three the condition was associated with monstrosities, that is, in each instance the fetus was malformed, which probably had something to do in causing the excess of amniotic fluid. In each instance the membranes were punctured in order to relieve the patient of her distressing symptoms. The same method was employed in the withdrawal of the fluid as described by Dr. Seeley, the membranes being punctured high up with a fine needle. The fourth case came on toward the end of pregnancy, the child being especially large. The membranes ruptured spontaneously, fortunately without prolapse of the cord.

It must be borne in mind that postpartum hemorrhage is quite common after hydramnios, either acute or chronic and must be guarded against. Chronic hydramnios is much more common than the acute form of the complication. Personally I have never seen good results from bandaging. Premature labor is very apt to result. With rupture imminent, puncture of the membranes is better than waiting, since spontaneous rupture is very apt to result in prolapse of the cord or malpresentation.

In reference to the case of Cesarean section, it seemed to me advisable with the deformity present to allow a test of labor. Even if the position of the fetus had not changed at the last, I do not believe the child could have been born alive by the natural passages, either with or without instruments. Elective Cesarean section at the beginning of labor before rupture of the membranes, in the absence of vaginal examinations, ought to be practically without mortality for both mother and child.

TRANSACTIONS
OF THE
CLINICAL SOCIETY
OF THE
UNIVERSITY OF MICHIGAN

STATED MEETING, FEBRUARY 11, 1914

THE PRESIDENT, R. BISHOP CANFIELD, M.D., IN THE CHAIR
REPORTED BY REUBEN PETERSON, M.D., SECRETARY

Reading of Papers

HOW BACTERIA CAUSE DISEASE.*

VICTOR C. VAUGHAN, M.D.
(From the Hygienic Laboratory, University of Michigan).

For about fifteen years my students and I have directed our attention and energy largely to the study of the chemistry of bacteria. This work has been collected, systematized and published in book form.* Early in our work we realized that in order to obtain enough cell substance in a pure state to enable us to study successfully its chemistry it would be necessary to devise some method for the growth of massive cultures. After several attempts we succeeded in perfecting the large copper double tanks which have proved wholly satisfactory and have supplied abundant growths, easily obtainable and free from contamination. A copper tank ten feet long, two feet wide, and four inches deep, with a trough around the edge one inch deep, has a cover which, when lowered into place, rests in the trough. This tank is supported by an iron frame of gas piping, the legs of which rest on rollers, so that the whole may be easily moved about the room. An inner tank, two inches shorter and two inches narrower, also provided with a trough that runs around the edge, sits in the large one, and is supported two inches from the bottom of the larger one by iron cross-bars. The bottom of the outer tank and the seal trough on the edges are filled with water. The seal trough of the inner tank is filled with glycerin. Both lids are raised and lowered by wire ropes passed through pulleys fixed in the ceiling. The iron frame supporting the tanks may be of any desired height. In our incubating room we have a nest of six tanks, three of which are on frames four feet high and three on frames two feet high. This economizes space, as the lower ones can be rolled under the higher ones. Both lids are supplied with vent tubes which are plugged with cotton in sterilization. Twenty liters of three per cent. agar is placed in the inner tank; both lids are lowered into their respective troughs, and with large gas burners at full blast underneath, the apparatus is a sterilizer. After three sterilizations on successive days the medium is inoculated by pouring a liquid culture through the vent tubes in the lid of the inner tank. Then with upper lid lowered into the water trough and gentle heat, which may be controlled by a thermoregulator, it becomes an incubator. With a number of tanks in a small room it is better to heat the room to the desired temperature, thus regulating the heat, than it is to heat each tank separately. (A photograph of this tank is shown in Fig. 1.)

After removal from the tanks the bacterial cellular substance may be washed with various fluids. As a rule, we have washed once or twice with sterile salt solution by decantation and then repeatedly with alcohol, beginning with 50 per cent. and increasing to 95 per cent. The substance is then placed in large soxhlets and extracted first for one or two days with absolute alcohol and then for three or four days with ether. These extractions with alcohol and ether should be thorough, in order to remove all traces of fats and waxes.

After extraction, the cellular substance is ground, first in porcelain, then in agate mortars, and passed through the finest meshed sieves. If there be bits of agar in the bacterial cellular substance, which is seldom the case, it is separated by the sieve and discarded. The one who grinds the cellular substance should wear a mask in order to protect himself; notwithstanding this precaution, several workers have been acutely poisoned, especially with the typhoid bacillus. Of course, there is no danger of infection, as the material, after the treatment already described, contains no living bacilli. The finely

*Protein Split Products in Relation to Immunity and Disease. Lea & Febiger. Philadelphia, Pa., 1913.

ground cellular substance in the form of an impalpable powder may be kept in wide-mouthed bottles in a dark place, and if so kept it retains its toxicity for years, but when long exposed to the light, even if kept perfectly dry, it becomes less poisonous.

With an abundance of bacterial cellular substance obtained from the tanks the following facts were established for the colon bacillus.

1. The poison is contained within the bacterial cell from which it does not, at least under ordinary conditions, diffuse into the culture medium.

2. The poison is not extracted from the bacterial cell by dilute salt solution, alcohol, or ether, at ordinary temperature or at the boiling point of these fluids.

3. The cellular substance of the colon bacillus may be heated with water without destruction of its poisonous group.

4. 0.5 per cent. solutions of the caustic alkalies disrupt the cellular substances of the colon bacillus slowly and imperfectly.

5. Boiling with a 0.2 per cent. dilution of hydrochloric acid has but little effect upon the bacterial cell or its contained poison.

6. Heating the cellular substance for an hour in an open dish on the water-bath, with from one to five per cent. hydrochloric acid, breaks up the cells and does not wholly destroy the toxicity of the cell content; however, prolonged boiling with one per cent. or stronger dilutions of hydrochloric acid does destroy the poison.

7. The bacterial cellular proteins are, so far as their toxicity is concerned, quite resistant to the action of pepsin and trypsin.

More thorough study of the bacterial cellular substances demonstrated the fact that the bacterial cell consists largely of complex proteins. It has been assumed that bacteria are low forms of vegetable life; our work, which has been confirmed recently in Kossel's laboratory, shows that this is not true and that bacteria, although simple morphologically, are highly complex chemically, in fact, bacteria are as complex chemically as the cells of our own bodies. This is a most important fact inasmuch as it shows that the bacterial cell and the body cell are much alike in chemical composition and, as we later demonstrated, that different kinds of bacteria differ in chemical composition. Bacteria are particulate proteins containing, at least two carbohydrate groups, a nuclein group and one or more protein groups; consequently when bacteria cells are disrupted they supply carbohydrates, nuclein bodies and amino acids.

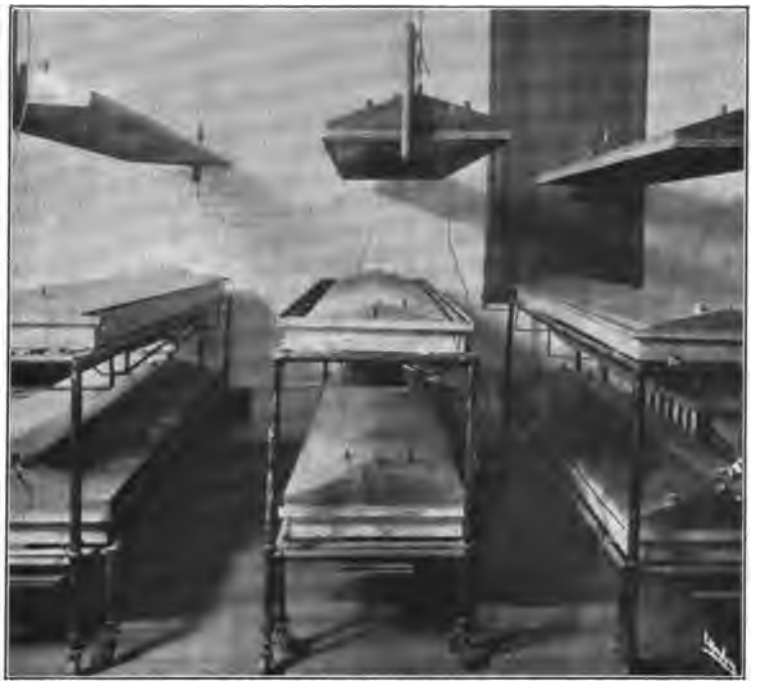

Fig. 1. The incubating room, lids raised.

After many failures we succeeded in splitting up bacterial cellular substances into poisonous and non-poisonous portions. We were able to do this not only with pathogenic but with non-pathogenic bacteria. Having found that bacterial cellular substances contain a highly active poison the question arose as to whether or not other proteins, bacterial, vegetable, and animal contain poisonous groups; moreover, we demonstrated that the poison obtained from all

these varieties of proteins has the same, or at least similar, action. Egg-white contains just as much poison and the same poison practically as that found in the tubercle bacillus.

A comparison of the effects of the living bacillus, the dead cellular substance, and the free poison is of great interest and throws much light on the phenomena of infection.

When a guinea-pig is inoculated with a fatal dose of the living colon bacterium, practically no symptoms whatever are noticeable for a period varying from six to twelve hours, according to the size of the dose given. This may be considered as the period of incubation and is roughly proportional to the amount of living culture injected. This period of incubation represents the time taken for the bacillus to multiply and to be destroyed to such an extent that sufficient poison may be liberated through its disintegration to produce recognizable effects in the animal. This period of incubation is in reality the crisis of the disease and the outcome depends on whether all bacteria have been destroyed before a fatal dose of the poison is set free. It is during this period that individual resistance and acquired immunity are important factors acting by causing increased destruction of bacilli before a fatal dose is set free. During this time the temperature of the animal may rise to a greater or less extent or may remain stationary; the animal is active and is in no way distinguishable from its untreated fellows. At the end of the period of incubation the animal becomes less active, it hangs its head, and apparently enters into a state of stupor; at the same time the temperature begins to fall abruptly, as can be seen by Fig. 2. The temperature will often fall from 101° to 94° F. or even lower within from two to four hours, and this fall is progressive and continues until the animal's death, immediately preceding which a temperature as low as 85° F. is not uncommon. At the same time the animal shows signs of peritonitis, as is evidenced by rigidity and spasms of the abdominal muscles on pressure. At autopsy, the only gross lesion present is a marked hemorrhagic peritonitis with a large amount of bloody fluid in the cavity.

On the injection of a fatal dose of the dead cellular substance intraperitoneally, the length of the period of incubation is shortened, in fact, we have cut out one of the processes of incubation, that is, the growth of the bacillus in the body, the bacillus has been grown artificially and enough of it has been injected into the animal to cause its death. Under ordinary conditions the period of incubation is determined by the length of time necessary for the body cells to disrupt the bacterial substance sufficiently to set free enough of the poison to produce recognizable effects. In the case of the guinea-pig treated with dead substance of the colon bacillus this period is reached in about four hours; at the end of this time the temperature begins to fall and there is a decided drop until time of death, provided the dose given is a fatal one. If a non-fatal dose has been injected the temperature, as will be seen from Fig. 3, has reached the minimum at the end of from six to eight hours and has returned to normal in from twelve to twenty hours. Accompanying the fall in temperature there is apparent lassitude, stupor and roughing of the coat. In cases in which many times the fatal dose has been given, the animals occasionally die within from four to six hours with convulsions, a feature which can now and then be observed after injection of large quantities of old living cultures. At autopsy we find a picture similar in all respects to that following inoculation with living bacillus. There is a marked hemorrhagic peritonitis, the peritoneal cavity containing

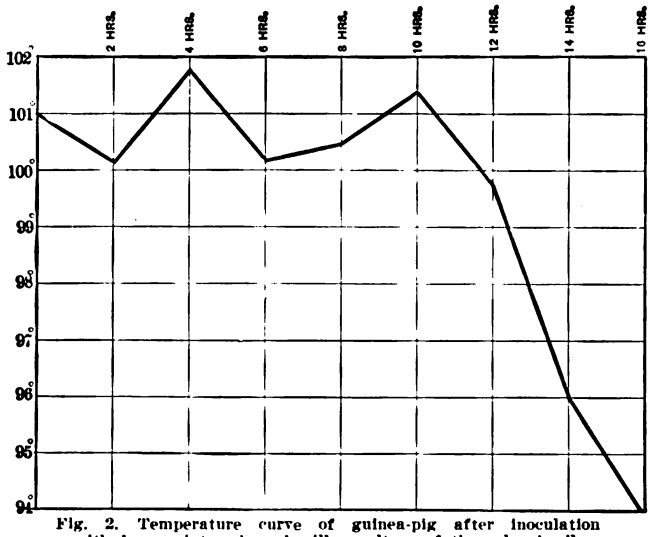

Fig. 2. Temperature curve of guinea-pig after inoculation with 1 cc., sixteen-hour bouillon culture of the colon bacillus. Death occurred twenty hours after inoculation.

bloody fluid, together with unabsorbed bacterial cell substance. From this we see that practically the sole difference between the effects following inoculation with the living bacillus and the injection of the dead bacterial substance is the shortening of the period of incubation due, no doubt, to the fact that the poison is liberated much more rapidly and in greater concentration in the second case. Since dead bacteria, both pathogenic and non-pathogenic, will kill animals when injected into the peritoneal cavity in sufficient amount it must be evident that the effects are not due directly to the growth of bacteria in the body; it must also be evident that whether a given bacillus is pathogenic or not does not depend upon its capability of forming a poison but upon its capability of growing and multiplying in the animal body.

When the free poison is given the temperature begins to fall within five to fifteen minutes and often it will be found to have reached 94° F. and even lower in many instances, (See Fig. 4). At first, after an interval of from five to ten minutes immediately following the injection, the animal appears restless, runs about the cage, and shows a great tendency to scratch itself, this undoubtedly being due to itching sensations in the skin caused by irritation of peripheral nerves. The animal then begins to show evidence of lack of co-ordination, which is rapidly followed by partial paralysis, which is especially marked in the hind extremities. This stage lasts for from five to ten minutes, during the latter part of which the animal usually lies quietly on one side. From this state the animal passes into what one might term the convulsive stage. These convulsions are usually clonic in nature and, as a rule, at first involve only the neck muscles, the head being momentarily drawn backward on the back. At first these convulsions are but slight in degree and are separated by considerable intervals of time. Soon, however, they become much more frequent and of much greater severity. Gradually they become more and more general in their extent. until all the muscles of the body become involved in violent clonic convulsions. This stage, when present, presages a fatal outcome; rarely an animal recovers after reaching the convulsive stage. During a convulsion, or occasionally in the interval of calm, respiration ceases. The heart, however, continues to beat, at first with perfect regularity and no acceleration; indeed, the rate seems to be somewhat slower than normal. Gradually the beat becomes more and more feeble, the rate and regularity being preserved to the end. It is usually only after an interval of from three to four minutes after the cessation of respiration that the heart ceases to beat. As has been previously stated, a fatal issue, if it occurs at all, always results within one hour after injection and usually within from thirty to forty minutes. This is to a large extent independent of whether the dose is the minimum lethal one or two or three times that amount. It is certainly entirely independent of the size of the pig. Death, of course, results at slightly different times with different batches of the poison, but even in this case the interval of time between injection and a fatal issue does not vary to any great extent. A dose which has proved to be the minimum fatal dose for one pig will almost surely prove to be the same for another. In other words, we have done away entirely with the period of incubation, and the poison acts so rapidly that individual resistance plays no part; hence, the animal acts almost with the exactitude of a chemical compound into which for all practical purposes it has been converted. The period of incubation has ceased to exist since the poison is no longer contained within either the dead or the living bacillus, but is present in a free and uncombined form, capable of uniting immediately with those body cells for which it may possess a special affinity.

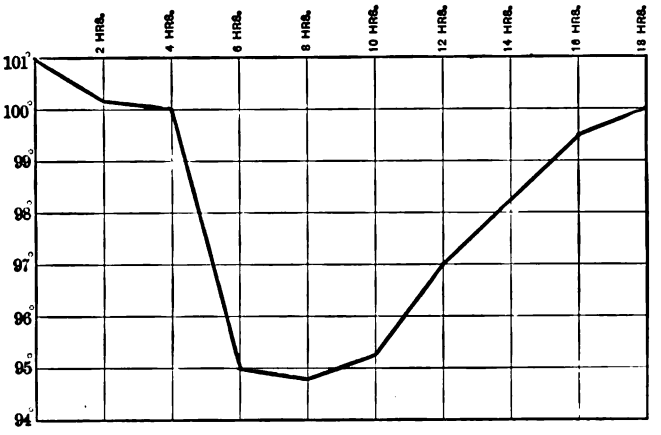

Fig. 3. Temperature curve of guinea-pig intraperitoneal injection of non-fatal dose of crude bacterial cell substance.

After the above described work had been

done, the phenomena of protein sensitization or so-called anaphylaxis became prominent and it will be necessary to discuss the elements of this discovery.

The older medical literature occasionally records facts which in the light of more recent and extended knowledge are known as the phenomena of protein sensitization. Such were some of the experiences recorded in the early attempts at the transfusion of blood. Many of the untoward results reached in the procedure and beyond the ken of that time are now fully explained. Behring and Kitashima[1] found on immunizing an animal to tetanus toxin that it died in convulsions notwithstanding the fact that the blood serum was richly charged with antitoxin. They explained this by assuming the existence of a condition of "hypersensitiveness" to the toxin. With our present knowledge we see no reason for ascribing this to the toxin. There is, so far as we know, no evidence that animals can be rendered hypersensitive to either toxin or antitoxin. Neither has ever been obtained free from proteins, and since all true proteins, so far as we know, sensitize, there seems no sufficient justification in ascribing a sensitization induced by a protein solution containing a toxin to the latter. Buchner[2] repeatedly injected bacterial proteins into men and noticed that the cardinal indications of local inflammation, tumor, rubor, dolor, and calor resulted. Furthermore, he noted that fever increased with repeated injections, Krehl and Matthes[3] induced fever in animals by repeated injections of albumose and peptone.

Weichardt[4] made an advanced study in the domain which we now designate as anaphylaxis. He repeatedly treated rabbits with protein expressed from placental cells, and found that some of these died promptly on subsequent injections. Furthermore, he mixed the serum of animals thus treated with placental cells and obtained a soluble poison which he named synzytiotoxin. Later, he showed that hay fever results from the parenteral digestion of the proteins of pollen. Both of these points will be discussed in more detail later. Wolff-Eisner[5] discussed the theory of endotoxins and their application to various diseased conditions, in a very suggestive manner, but added little to our exact knowledge. Richet[6] has made many valuable contributions to this subject. In his first report made with Portier in 1902, he worked with an extract from the tentacles of a muscle and showed that an injection of this made the animal much more susceptible to a second one. Unfortunately, he coined the word anaphylaxis as most suitable to cover this condition of increased susceptibility. He used this word understanding it to mean "without protection," indicating that the first injection destroyed any natural resistance that the animal might possess against the poison. Now, we know that the condition of sensitization is essential to certain forms of immunity, as was first indicated by Vaughan and Wheeler,[7] and the inappropriateness of the term anaphylaxis is self-evident. However, the word has come into general use, and with this explanation we will continue it. V. Pirquet[8] proposed and has continued the use of the word "allergie," meaning altered energy. This is much more suitable, inasmuch as it simply expresses a fact and binds no one to any theory. However, "allergie" has not been usually employed, and we will use "protein sensitization," "hypersensitiveness," "anaphylaxis," and "allergie" as synonyms.

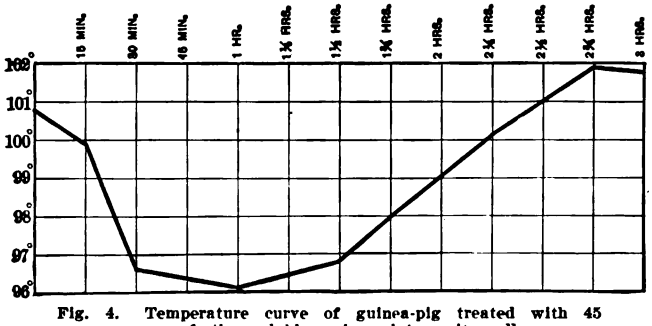

Fig. 4. Temperature curve of guinea-pig treated with 45 mgs. of the soluble poison intraperitoneally.

The fact that animals which have once received an injection of protein are liable to sudden death after a second injection of the same kind has been known for many years. Ever since the opening of the Hygienic Laboratory of the University of Michigan (1888), animals once used have been segregated and kept in cages marked "used animals," which indicated that conclusions could not be safely drawn from re-

1. Berl. klin. Wchnschr., 1901.
2. Berl. klin. Wchnschr, 1890, 216; München. med. Wchnschr., 1891.
3. Arch. f. exper. Path. u. Pharmak. 1895, XXXV, 232; ibid., 1896, XXXVI, 437.
4. Berl. klin. Wchnschr., 1903.
5. Zentralbl. f. Bakt., 1904, XXXVII, München. med. Wchnschr., 1906, Dermat. Zentralbl., 1906, Berl. klin. Wchnschr., 1907.
6. Compt. rend. Soc. de biol., 1902, Ann. de l'Inst. Pasteur, 1907, XXI, 497; ibid., 1908, XXIII, ibid, 1909.
7. Jour. Infect. Dis., 1907.
8. München. med. Wchnschr., 1906.

sults obtained when these animals were employed a second time. In the standardization of diphtheria antitoxin it soon became evident that the guinea-pig that survives one test could not be relied upon in a second one. In the late nineties, Parke, Davis & Co., large manufacturers of antitoxins, ascertained this fact and offered to supply the Hygienic Laboratory of the University of Michigan with "used" guinea-pigs at a small price. The offer was accepted, but the animals were found dear at any price, as they suddenly and unexplainably died when treated with horse serum.

This condition evidently was observed by others, and Theobald Smith mentioned it to Ehrlich, who set Otto to work to find the explanation. Otto[9] published his results under the title "Das Theobald Smithsche Phänomen der Serumüberempfindlichkeit." However, simultaneously with these observations on animals used in the standardization of antitoxin, the profession had occasion to observe the effects of injections of antitoxin in human beings. As early as 1903, v. Pirquet[10] wrote concerning certain clinical effects following antitoxin treatment, and in 1905 he and Schick published a monograph "the serum disease," "Die Serumkrankheit."

Friedemann[11] offers the following definition: "We speak of anaphylaxis when the organism, in consequence of a previous treatment with an antigen, after a period of incubation becomes hypersensitive to the same or to a closely related substance, and when this condition can be passively transferred to fresh animals by the serum or organ extracts of the sensitized animal." Biedl and Kraus,[12] omitting passive anaphylaxis, give the following: "By anaphylaxis we mean *that* state of specific hypersensitiveness induced in animals by protein injections, and in which symptoms of poisoning follow subsequent injections of the same protein in doses which would have no effect upon untreated animals." With some explanation to be given later we accept these definitions as quite satisfactory. In the meantime it is desirable to have a clear understanding of the meaning of the terms employed in discussing this subject. The substance which induces the anaphylactic state is generally known as the "antigen." This implies that it gives rise to the production of an antibody, and the selection of this word has been determined by an attempt to correlate the phenomena of anaphylaxis with the theory evolved by Ehrlich in explanation of the production of antitoxins by treatment with toxins. In truth the "antigen" of anaphylaxis is not a toxin, nor is the new substance generated in the body of the treated animal an antitoxin. The term "anaphylactogen" is unobjectionable, since it is applicable to any substance which induces the anaphylactic state. Sensitizer is a good word, and commits one to no theory. The same is

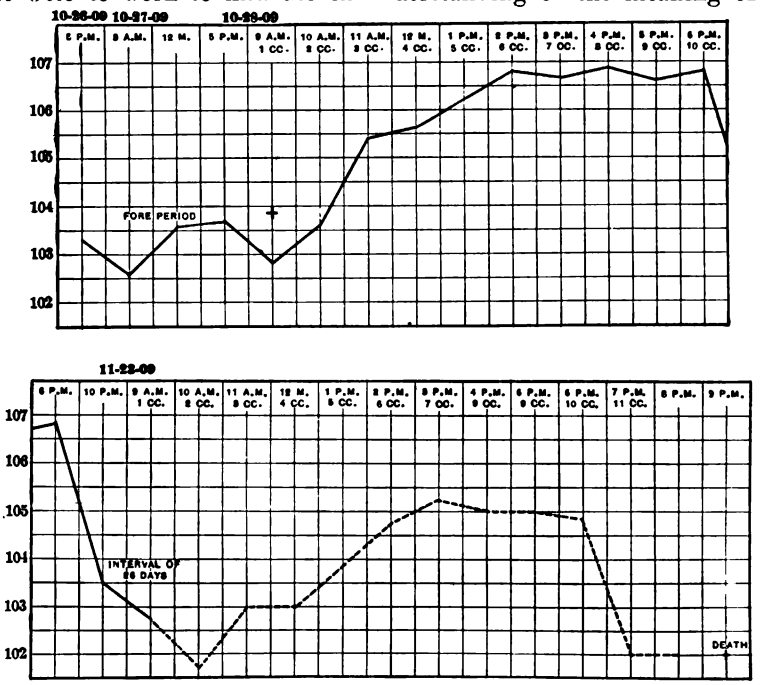

Fig. 5. Acute fever produced in a rabbit by intravenous injections of egg-white. The continuous line represents the temperature in the non-sensitized animal. The broken line represents the temperature in the same animal, sensitized.

9. v. Leuthold: Gedenkschrift. 1906.
10. Wien. klin. Wchnschr.
11. Jahresb. ü. d. Ergebn. d. Immunitätsforschung. 1910. VI.
12. Kraus and Levaditi: Handbuch d. Technik u. Methodik d. Immunitätsforschung. Ergänzungsband.

true of the term "sensibilisinogen" used by our French Confreres. The sensitizer causes the body cells of the treated animal to elaborate a specific proteolytic ferment which digests or splits up the sensitizer. Again, following the nomenclature of Ehrlich, this ferment elaborated as a consequence of the introduction of the sensitizer is generally designated as the "antibody." It would be equally rational to speak of pepsin as an antibody of beefsteak, because the former digests the latter. The theory evolved by Ehrlich in his studies on toxin immunity is the product of a genius of the highest order. It has stimulated research, which has resulted in discoveries of the greatest importance, but the attempt to explain all physiologic and pathologic processes by this theory, and to describe them in the nomenclature of this theory is unscientific. To say that anaphylaxis is the result of protein-antiprotein reaction is to talk jargon. When foreign proteins are taken into the alimentary canal they must be digested before they are absorbed. This means that their large molecules must be split into smaller ones, and this must be continued until there are no more protein molecules left. Every protein molecule contains a poisonous group, and in normal, alimentary digestion this group is rendered nonpoisonous by further cleavage before absorption takes place. When foreign proteins find their way into the blood and tissues they must be digested. This is accomplished, as it is in the alimentary canal, by proteolytic ferments but the danger from the poisonous group in the protein molecule is evidently greater in parenteral than in enteral digestion. Both enteral and parenteral digestion are physiologic processes. Every living cell has its own proteolytic ferments, otherwise it could not live. When stimulated it pours out this ferment, and it does so only when stimulated. The function of a cell ferment depends upon the kind of cell elaborating it, and to a certain extent upon the stimulating substance. The proteins are the normal stimulants to cell secretion. When a foreign protein is introduced into the blood or tissue it stimulates certain body cells to elaborate that specific ferment which will digest that specific protein. When such a protein first comes in contact with the body cells the latter are unprepared to digest the former, but this function is gradually acquired. The protein contained in the first injection is slowly digested, and no ill effects are observable. When subsequent injections of the same protein are made, the cells, prepared by the first injection, pour out the specific ferment more promptly and the effects are determined by the rapidity with which the digestion takes place. The poisonous group in the protein molecule may be set free so rapidly and in amount sufficient to kill the animal. This in brief is an explanation of the phenomena of anaphylaxis.

In 1907 Wheeler and I proposed a theory of sensitization, the principles of which may be stated as follows:

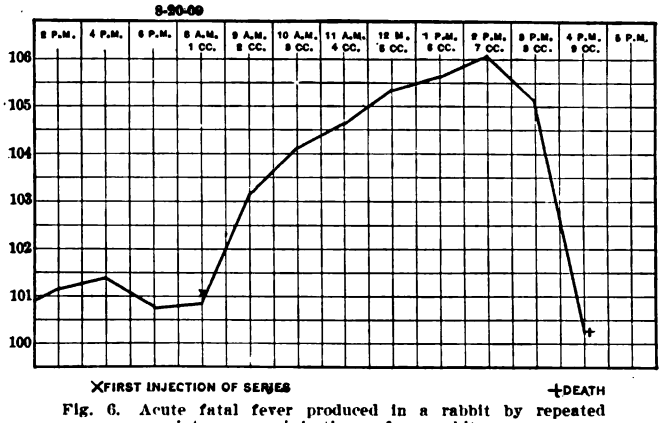

Fig. 6. Acute fatal fever produced in a rabbit by repeated intravenous injections of egg-white.

1. Sensitization consists in developing in the animal a specific proteolytic ferment which acts upon the protein that brings it into existence, and no other.

2. This specific proteolytic ferment stored up in the cells of the animal as a result of the first treatment with the protein remains as a zymogen until activated by the reinjection of the same protein.

3. Our conception of the development of a specific zymogen supposes a rearrangement of the atomic groups of the protein molecules of certain cells, or an alteration of their molecular structure. In other words, we regard the production of the specific zymogen not as the formation of a new body, but as resulting from an alteration in the atomic arrangement within the protein molecule, and a consequent change in its chemism.

4. Some proteins in developing the specific zymogen produce profound and lasting changes in molecular structure, while the alterations induced by others are slighter and of temporary

duration, the molecular structure soon returning to its original condition.

5. Bacteria and protozoa are living, labile proteins, while egg-white, casein, serum albumin, etc., are stabile proteins. The proteins of one group are in an active, while those of the other are in a resting state, but both are essentially proteins made up of an acid or poisonous chemical nucleus, and basic, non-poisonous groups. Bacterial immunity and protein sensitization, apparently antipodal, are in reality the same, and each consists in developing in the animal body the capability of splitting up specific proteins. If the living protein be split up before it has time to multiply sufficiently to furnish a fatal quantity of the poison, the animal lives and we say it has been immunized. If the stabile protein be introduced into the animal body it leads to the development of a specific proteolytic ferment, and if enough of it to supply a fatal dose be reinjected after this function has been developed, the animal dies.

gether tends to resist this process of disintegration. The pathogenic bacterium assimilates the nutritious constituents of the fluids of the animal body, builds them into its own tissue, converts them into substances foreign to the host, and finally, when the bacterial cell goes to pieces either from spontaneous dissolution, or through the aggressive action of some animal cell, these reconstructed chemical groups are set free and poison the animal, inducing lesions in various tissues, and, in many instances, so interrupting the vital functions as to cause death. It is in harmony with these statements that Friedberger has been able to induce aseptic pneumonia by spraying horse serum into the lungs of guinea-pigs sensitized with the same, and Schittenhelm and Weichard have established "enteritis anaphylactica" by the reinjection of egg-white into sensitized dogs. It is more than probable that cholera infantum and the kindred summer diarrheas result from the absorption of undigested milk and consequent sensitization. The designation "protein disease" might be used to cover the majority of bacterial and protozoal disease, and many of these hitherto regarded as autogenous.

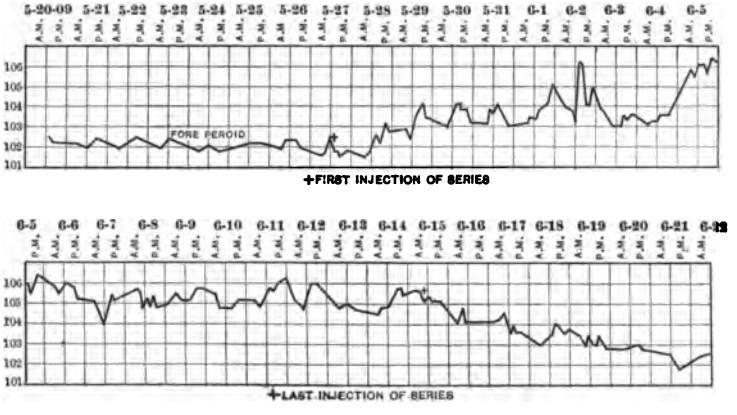

Fig. 7. The production of continued fever in a rabbit by repeated subcutaneous injections of egg-white.

6. We are compelled to change our ideas concerning the causation of the lesions of the infectious diseases. Formerly, we believed the structural changes to be due wholly to the living, growing, feeding microörganisms. For instance, we were sure that the intestinal ulcerations of typhoid fever are caused by the living bacilli. Now we know that these lesions follow the intravenous injection of dead proteins. As has been stated, each foreign protein has its predilection tissue in which it is largely deposited, whose cells it especially sensitizes, and where it is disrupted. This explains the characteristic lesions and symptoms of the different infectious diseases. Bacterial inflammation is essentially a chemical process, or is due to the disruption of cell molecules through the chemical affinity between certain groups in the bacterial cell and certain groups in the cell of the animal. So long as the bacterial cells are alive the chemism that holds the living molecule to-

7. It seems to be a physiologic law that the specific ferments elaborated by living cells are determined by the proteins brought into contact with them, but as yet we know but little concerning these bodies which we call ferments. That they are labile chemical bodies resulting from intramolecular rearrangement in the protein molecules of the cell seems a plausible theory, but at present it is only a theory. We know but little of the action of these so-called ferments upon their homologous proteins. Our knowledge of the chemistry of protein sensitizers is exceedingly limited, and, as we have pointed out, it is highly desirable that work in this direction should be prosecuted with vigor, because we need sensitizers free from the poisonous group. Furthermore, there is the question

why small doses of protein induce fever while large doses have no such effect. At present we have no satisfactory answer to this question. If it could be conclusively demonstrated that the toxins are ferments, the subject of the etiology of disease would be greatly simplified. We have elsewhere, given our reasons for holding that the toxins are ferments, and at this point we wish to formulate what we believe to be two biologic laws:

(a) When the body cells find themselves in contact with, or permeated by, foreign proteins they tend to elaborate specific ferments which digest and destroy the foreign proteins.

(b) When body cells are attacked by destructive ferments they tend to elaborate antiferments, the function of which is to neutralize the ferments and thus protect the cells.

In 1909, Wheeler, Gidley and I demonstrated that any desired form of fever, acute, fatal, continued, intermittent, or remittent can be induced in animals by regulating the size and frequency of the doses of foreign protein administered parenterally, and in 1911 Cumming, Wright and I extended the details of this work. As a result of these studies we reached the following conclusions:

1. Large doses of unbroken protein administered intra-abdominally, subcutaneously, or intravenously have no effect upon the temperature; at least do not cause fever.

2. Small doses, especially when repeated, cause fever, the forms of which may be varied at will by changing the size and the interval of dosage (for fever charts see Figs. 5, 6 and 7).

3. The effect of protein injections on the temperature is more prompt and marked in sensitized than in fresh animals.

4. The intravenous injection of laked blood corpuscles from either man or the rabbit causes in the latter even in very small quantity, either in single or repeated doses, prompt and marked elevation of temperature.

5. Laked corpuscles after removal of the stroma by filtration have a like effect.

6. Protein fever can be continued for weeks by repeated injections, giving a curve which cannot be distinguished from that of typhoid fever.

7. Protein fever is accompanied by increased nitrogen elimination and gradual wasting.

8. Protein fever covers practically all cases of clinical fever.

9. Animals killed by experimentally induced fever may die at the height of the fever, but, as a rule, the temperature rapidly falls before death.

10. Fever induced by repeated injections of bacterial proteins and ending in recovery is followed by immunity.

11. The serum of animals in which protein fever has been induced digests the homologous protein in vitro.

12. Fever results from the parenteral digestion of proteins.

13. There are two kinds of parenteral proteolytic enzymes, one specific and the other non-specific.

14. The production of the non-specific ferment is easily and quickly stimulated.

15. The development of the specific ferment requires a longer time.

16. Sensitization and lytic immunity are different manifestations of the same process.

17. Foreign proteins, living or dead, formed or in solution, when introduced into the blood soon diffuse through the tissues and sensitize the cells. Different proteins have predilection places in which they are deposited and where they are, in large part at least digested, thus giving rise to the characteristic symptoms and lesions of the different diseases.

18. The subnormal temperature which may occur in the course of a fever or at its termination is due to the rapid liberation of the protein poison, which in small doses causes an elevation, and in larger doses a depression of temperature.

19. Fever *per se* must be regarded as a beneficent phenomenon, inasmuch as it results from a process inaugurated by the body cells for the purpose of ridding the body of foreign substances.

20. The evident sources of excessive heat production in fever are the following: (a) That arising from the unusual activity of the cells supplying the enzyme; (b) That arising from the cleavage of the foreign protein; (c) That arising from the destructive reaction between the split products, from the foreign and the proteins of the body.

From the work already detailed I have formulated statements concerning the phenomena of infection. These may be briefly stated as follows:

In all infections there are two principal factors—one the infecting virus and the other the body cell. In addition to these there is the environment in which the struggle for supremacy between the virus and the body cell takes place. This consists of the unorganized fluids of the body, and is of great weight in determining the result of the contest. In the first place, what do we know of the infecting virus? As we have seen, bacteria are particulate, specific proteins. Since they are particulate, we speak of them as bacterial cells. It is not, however, essential that an infecting virus be participate in the sense that it be possessed of substance and form recognizable to our limited sense of sight even when aided by the most perfect microscope. There are many filterable viruses. Some pass through our finest porcelain filters

and cannot be deposited from the fluids in which they exist even when kept for hours in the most efficient centrifuge manufactured. Theoretically, there is no reason why a virus may not exist in any degree of lability of structure. The bacteria are particulate and solid, which means that their structure is so radically different physically from the medium in which they exist that they can be recognized by sight, aided by proper magnifying lenses, but viruses may be semi or wholly fluid. In such instances their structure is not sufficiently differentiated from the medium that we can recognize them. According to our conception, a living protein does not necessarily possess a form recognizable to our limited sense even when aided by the most perfect lenses.

One of the most important results of our work, in our opinion, is the demonstration that bacteria are chemically not simple, but quite complicated in structure. Morphologically, they show but little or no differentiation in structure, but chemically they are quite as complicated and complex as many of the cells of higher animals. They contain carbohydrates, nuclein bodies, and polymers of the mono- and diamono-acids. They are glyconucleo-proteins. We interpret this as signifying that functionally they are highly developed.

While an infecting virus may be solid, semi-solid, gelatinous, or liquid, we will, in the further consideration of the phenomena of infection, take the particulate type, the bacterium, as an example of an infecting agent.

What are some of the capabilities of a bacterial cell? In the first place it possesses that attribute which distinguishes and characterizes all living matter—the capability of growth and reproduction. In order to grow and multiply its molecular structure must be labile- in a state of constant change. Some bacteria under certain conditions may pass into a resting state characterized by the formation of spores, but these are awakened into life when the environment becomes fit, and the spore develops into the active form when it infects. In all instances the active, infecting agent is a living protein, capable of growth and multiplication. In order to do this it must carry on a constant exchange in matter with the medium in which it exists. It must assimilate and eliminate. It must absorb groups from the molecules about it, and cast out those which it has already used. Stop this process and the continuation of life is impossible. Every living cell, be it bacterial, vegetable, or animal, must feed or cease to exist. Besides, a cell is limited in its food supply by that which lies within its reach. There must, therefore, be a certain supporting relation between the bacterial cell and the medium. The groups derived from the medium must fit into the molecular structure of the cell, otherwise they would be of no service to it. This necessitates the cleavage of the molecules of the medium along definite lines. Many kinds of cells may live in the same or like media, but for each kind of cell the cleavage of the medium must be specific. From this it follows that the agent by which the cleavage products are secured must be supplied by the cell itself, and must be peculiar to that kind of cell. These cleavage agents which prepare foods for the cell from the medium are known as ferments, and each kind of cell has its own characteristic and specific ferments. As to the real nature of ferments, we know little or nothing, but that every kind of cell has its specific ferment or ferments, we do know. The same ferment may not be able to break up all proteins. In this respect there are great variations in the proteolytic ferments. Some digest a wide variety of proteins while others are capable of acting only on one specific protein. There must be a relation between the ferment and its substrate. As Fisher once said, the former must fit the latter as a key fits into the lock, and as there are master keys that open many doors, so there are general proteolytic ferments, and as there are special keys that fit only one lock, so there are specific proteolytic ferments. It will be observed that we have used the word "specific" in two senses in speaking of proteolytic ferments. Each kind of cell has its specific ferment, and each protein may have its specific ferment. This double use of the term "specific" should be borne in mind, since there seems to be no way to avoid it.

It follows from what has been said that a bacterium placed in a medium in which its ferment is ineffective cannot grow and multiply. A bacterium which cannot grow and multiply in the animal body cannot cause an infection. Its inability to grow and multiply in the animal body may be due to the fact that its ferment or ferments cannot digest or properly break up the proteins of the animal body. This is one of the reasons why the great majority of bacteria are non-pathogenic or are harmless. These organisms when grown on suitable media produce as much poison as the pathogenic bacteria, but not being able to feed upon the proteins of the body they die. This, however, is not the sole, and probably not the most important, cause of the failure of so many varieties of bacteria to do harm to the higher animals. What has been said about the production of ferments by the bacterial cell is equally true of the body cell. In fact, it is true of every living cell. The body cell has its specific ferments, and the bacterial cell being protein substance is liable to be digested by the ferments elaborated by the body cells.

In the inability of the bacterial cell to grow in the animal body either because it cannot feed upon the proteins of the body, or because it is

itself destroyed by the ferments elaborated by the body cells lies the fundamental explanation of all forms of bacterial immunity either natural or acquired. Toxin immunity needs further explanation. Certain bacteria, of which the diphtheria bacillus may be taken as a type, elaborate solable, extracellular substances known as toxins. These are probably ferments or closely allied bodies. They resemble ferments in the following particulars: (1) They are destroyed by heat. (2) They act in very dilute solution. (3) When repeatedly injected into animals in non-fatal doses they cause the body cells to elaborate antibodies which neutralize the toxin both in vivo and in vitro. (4) In the development of their effects a period of incubation is required. (5) It has been shown by Abderhalden, by optical methods, that they have a cleavage effect upon proteins. They split complex proteins into simpler bodies. In other words, they have a proteolytic action. (6) They are specific in two senses. (a) They are specific according to the cell which produces them. Diphtheria toxin is elaborated by the diphtheria bacillus and by no other organism. The toxin of snake venom is a specific conduct of the poisonous gland of the snake, and this is further specific inasmuch as that produced by the glands of one species is different from that elaborated in another species. (b) They are specific in the antibody elaborated in the animal body after repeated injections of non-fatal doses. Diphtheria antitoxin protects only against diphtheria toxin, and not against that of the tetanus or dysentery bacillus, or that of snake venom.

The side-chain theory evolved by the genius of Ehrlich best explains the action of toxins and the production of antitoxins. Without subscribing to all the details of this theory, we believe that it is a biologic law that when a living cell is attacked by a destructive ferment or toxin it tends to elaborate an antiferment or antibody. This is one of the ways in which the living cell may protect itself. The formation of such antibodies in multicellular animals is one of the factors in the fine adjustment essential to harmony of action between different tissues and organs. It best explains the fact that the digestive organs do not harm themselves, and the antitryptic action of blood-serum is one of the most interesting and important phases of parenteral digestion.

The number of pathogenic bacteria which produce toxins, at least in appreciable quantity, is small, and the action of toxins and antitoxins in infections due to those organisms which do not produce such bodies is of minor importance. Since all bacteria, and in fact all living cells produce ferments, and since every ferment, so far as we know, may lead cells acted upon by them to produce antiferments, there may be some toxin and antitoxin action in all infections, but in most bacterial infections such action is overshadowed by processes much more powerful in their effects.

In our opinion the action of the diphtheria bacillus may be stated as follows: The organism finds lodgement and the conditions for growth favorable in the upper air passages. Here it grows in mass and may kill by mechanical obstruction. It produces its soluble, diffusible toxin, which has the properties of a ferment and splits up the proteins of the body, setting free the protein poison. In case of recovery or in the production of antitoxin in animals, the body cells elaborate an antiferment or antitoxin which neutralizes the toxin and prevents its cleavage action. The bacilli in the throat are not destroyed by natural recovery or by cure with antitoxin, but the action of the toxin is prevented by the antibody. It is not, in our opinion, the toxin itself which kills, but a cleavage product which results from the action of the toxin on the proteins of the body.

All ferments are of cellular origin. This does not mean that ultramicroscopic forms of life or non-participate living organisms, if there be such, do not produce ferments. It would probably be better to say that all ferments are the products of living organisms and that there can be no living organism which does not produce its specific ferment. We cannot conceive of life without ferment action, because all living things must feed and food assimilation without ferment action is inconceivable. Food must be fitted for assimilation, and this is dependent upon ferment action.

Ferments are intra- and extracellular. All are formed within the cell, but some diffuse into the medium while others do not. In some instances at least cell permeation by the pabulum is essential to the feeding of the cell. In other instances it is highly probable that the ferment is accumulated on the cell surface and there acts upon the pabulum. In still other instances the ferment diffuses into the medium more or less widely from the cell which elaborates it. Many cells produce both intra- and extracellular ferments, and these are not necessarily the same. In some instances, probably in most cells, the intracellular ferment cannot be extracted from the cell or obtained in soluble form without destruction of the cell. This does not mean that it must exist in the soluble form before it can manifest its cleavage action. The pabulum may permeate the cell and in this location be split up by the intracellular ferment. We have insisted upon this as an explanation of the well-established fact that soluble proteins sensitize much more readily and completely than insoluble ones.

Before proceeding further it may be well to call special attention to some of the properties

of these ferments. The extracellular ferments are diffusible. They not only pass out of the cells in which they are prepared, but they diffuse more or less widely through the medium which surrounds the cell. This suggests that in molecular structure they are relatively simple. At least some of them may pass through membranes and collodion sacs, as is shown by the fact that bacteria and other proteins enclosed in such receptacles and left in a body cavity are destroyed. The extracellular ferments are, in part at least, filterable, passing with more or less readiness through porcelain. In their activities they are easily affected by modification in the medium through which they diffuse. The alexin of the blood serum is highly sensitive to the salt content of the serum, and by variations in this the activity of the ferment may be hastened, lowered, or wholly arrested. The same is true of bacterial ferments. In one species of animal a given bacterium multiplies with great rapidity; in another it grows slowly, while in a third it cannot grow at all. There are like variations in individuals of the same species. The extracellular ferments, at least some of them, are susceptible to slight changes in temperature. It is believed that every ferment has its optimum temperature, but the range in which continued activity is possible is narrow with some and relatively wide with others.

The intracellular ferments are non-diffusible, or at least less diffusible than the extracellular. They remain in the cells in which they are elaborated. They cannot be extracted from the cell by indifferent solvent. As a rule, they can be obtained from the cell only after partial or complete destruction of the cell. Some, probably most, are best extracted from the cell with dilute alkali, while others are best obtained by dilute acid. In either case the reagent must not be strong enough to destroy the ferment itself. They are non-filterable, or pass through filters slowly and imperfectly. We suspect that their molecular structure is relatively complex, or that they are more colloidal than the extracellular ferments. Under natural conditions the intracellular ferments act only on those bodies which are taken into the cell. The inclusion of bacteria by phagocytes is essential to the digestion of the former by the intracellular ferment of the latter. This is a phenomenon which may be seen, but cell permeation by foreign bodies is certainly necessary before such bodies can be acted upon by the intracellular ferments, and occurs with soluble proteins as well as with particulate ones. The intracellular ferment bears a wider variation in temperature, and is not so easily and delicately influenced by variations in the composition of the medium in which the cell exists. So far as we know the intracellular ferments do not diffuse from living cells. They are, however, recognizable in the fluids of abscess cavities as the leukocytes disintegrate. We are of the opinion that they are essential constituents of the chemical structure of cells. The reason for this belief will be developed later. The extracellular ferments may be regarded as secretions of cells. Much has been written about cellular and humoral theories. In our opinion every living thing has a chemical structure, which we may designate as a cell if we wish, understanding that a cell is not necessarily something that can be seen, and that it may possess widely different degress of liability, but we are quite certain that there is no ferment which is not the product of life processes. We have been somewhat surprised to find it stated that our own theory of protein sensitization or anaphylaxis is a humoralistic doctrine.

All ferments are products of life processes, and all life processes are more or less responsive to outside influences, to change in environment. In our opinion the most valuable fact that we have learned in the study of protein sensitization is that life processes manifested through ferment action are modified and may be modified at will by changes in environment. The blood-serum and organ extracts of normal guinea-pigs do not digest egg-white, but these fluids from an animal sensitized to this protein do have this action. The virus of smallpox is pathogenic to the man who has never had smallpox, and has not been vaccinated, but to the man who has had the disease or been properly vaccinated the virus of smallpox is non-pathogenic. We explain this, and in our opinion, the experiments of v. Pirquet have so demonstrated, that this is due to the fact that the ferments of the man's body cells have been so influenced by the disease or by vaccination that they have acquired a new function—that of digesting and thus destroying the virus of the disease. If this explanation be true, it opens up a wide field for the possible extension of the beneficial effects of preventive treatment.

There is another point of difference between intracellular and extracellular ferments, which is of the greatest importance in a study of the phenomena of infection. The extracellular ferments are comparable to those of the digestive juices of the alimentary tract in the higher animals. They roughly prepare foods for the cells. Their function is solely a lytic one. They break up complex proteins into simpler bodies, but the products thus formed are not, without further treatment, ready to be built into the structure of the cell. Proteins in the medium are rendered soluble by the extracellular ferments. They are so altered that they may be taken into the cell, but they are not so patterned that they are ready to be built into the struc-

ture. They are fitted for absorption, but are not ready for assimilation. The extracellular ferments are in a sense destructive agents. They break down complex molecules into simpler structures. The intracellular ferments are constructive. They are cell builders. They shape the material brought them and fit it into place. They build up specific proteins. They convert the raw material brought them into specific proteins, bacterial, vegetable, or animal. This does not mean that the intracellular ferments have no cleavage action. They chip the rough stone so that it fits in at the right place. It is by virtue of their activity or through their agency that cells grow and multiply. In case of an infectious disease the intracellular ferment of the infecting organism during the period of incubation converts man's proteins into bacterial proteins, and continues to do this with more or less success during the course of the disease. This seems to be accomplished in some diseases, at least, like typhoid fever, without any marked disruption of the cells of the man's body. The bacteria multiply rapidly during the period of incubation, and at this time the man is unconscious of the fact that his body is serving as a culture flask. We must conclude from this that the conversion of human proteins into typhoid proteins in the growth of the infecting agent is not accompanied by the liberation of the poisonous group in the protein molecule. This group, probably attached to other groups, or as a constituent of a more complex group, is used in the construction process. The poisonous group is common to all proteins. The synthesis of specific proteins from other specific proteins is accomplished without the liberation of the poisonous portion. It is one of the building stones, and changes in specificity do not occur in this, but in the secondary or characteristic group. This is, in our opinion, the explanation of the fact why incubation—a period of rapid reproduction in the infecting agent—proceeds without any recognizable disturbance in the health of the host. The typhoid bacillus, therefore, does not feed upon the cells of the man's body, but upon the formless, soluble proteins. Cell building is accompanied by the absorption of the poisonous group in the proteins serving as food. However, when the body cells become sensitized and elaborate a ferment which breaks down the bacterial cells, the poisonous group in the proteins of the latter is set free, and it is the effect of this poison that develops the symptom complex of the disease. The symptoms of one infectious disease differ from those of another largely according to the organ or tissues in which the infecting agent is located. In acute miliary tuberculosis and in typhoid fever, both conditions arising from a bacteremia caused by different organisms, the symptoms are only too frequently identical, and it is only by bacteriologic methods, a suggestive history, or the findings of a pre-existing tuberculous focus in some part of the body that a differential diagnosis may be reached. A cholecystitis is the same, not only in symptomatology, but frequently in gross pathology as well, whether the infecting organism be the pneumococcus, the streptococcus, the colon, or the typhoid bacillus. The most skillful diagnostician cannot tell from the symptoms alone the specific bacterial cause of a meningitis.

During the period of incubation of an infectious disease, the infecting organism supplies the ferment, the body proteins constitute the substrate, the process is essentially constructive, no poison is set free, and there are no recognizable clinical symptoms. During the active progress of an infectious disease, the body cells supply the ferment, the infecting organism constitutes the substrate, the process is essentially destructive, the protein poison is set free, the symptoms of disease appear and life is placed in jeopardy.

Our work seems to show that the body cells, when overwhelmed with a foreign protein of the blandest kind—such as egg-white—may fail to function and death may result. There is no reason for suspecting that in these cases there is any cleavage of the foreign protein or the liberation of any poison. The body cells are simply clogged with the foreign protein and fail to function. We are not sure that this phenomenon has any parallel in the infectious diseases. There is, however, something closely related to it in cholera infantum, cholera nostras, and Asiatic cholera.

We have already referred to the fact that ferments may be modified in their activities. These modifications may be so radical that it is generally believed that cells may be trained, as it were, to develop new ferments. There can be no doubt that change in environment does alter activity as manifested through the ferments. As we have stated, it seems to be a biologic law that when a living cell is brought in contact with or permeated by a foreign protein, it tends to furnish a ferment which will digest and destroy the foreign body. The ferments of the cells of man's body may be modified or new ones developed by (a) disease, (b) vaccination, and (c) sensitization. Many of the infectious diseases give immunity to subsequent exposure. In some of the chronic infectious diseases the altered behaviour of the body cells to the infecting agent is evident even while the disease continues.

DISCUSSION.

Dr. J. H. Agnew: I have nothing to add that would be of any particular interest. I am always glad to hear Dr. Vaughan speak of this work, because I had the privilege of working with him, isolating some of the amino-acids of the cell substance of the colon

and tubercle organisms. It appears from Dr. Vaughan's remarks this evening that this feature, the structure of the protein of bacterial cellular substance, is of prime importance. It has been thought that bacterial proteins were simple substances but it has been shown in Dr. Vaughan's laboratory that they are quite as complex as proteins from other sources and therefore the same phenomena may be expected from them as from other proteins.

PROGRESSIVE BULBAR PALSY, ASTHENIC TYPE. (MYASTHENIA GRAVIS).

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(From the Clinic for Diseases of the Nervous System, University Hospital, Ann Arbor, Michigan).

A woman, age thirty-nine years, was admitted to the Hospital of the University of Michigan on February 5, 1914, complaining of marked difficulty in speech and deglutition. Her family history was negative; no member of her family, a large one, had any similar condition. She had an appendiceal abscess when twenty-five years old and was operated upon. The following winter she had "peritonitis." Menstruation began at fourteen, was regular but painful, sometimes accompanied by syncopal attacks. She was married at thirty and five years later gave birth to a dead fetus. Following her pregnancy the menstrual periods were less painful. While still in childbed she began having attacks of epigastric pain, nausea and vomiting, diagnosed later as due to "achylia gastrica and cholecystitis." She suffered from attacks of this sort until March, 1912, when she had the last one. Her present trouble began about one week after the last attack of the vomiting, when she noticed at dinner a difficulty in swallowing and a husky voice. Since then the condition has grown progressively worse except for an interval of a week about Christmas, 1913, when there was a slight remission. She had been in bed for ten weeks on account of her general weakness and has had to be tube fed for about the same length of time. There has been no pain in any part of the body at any time during this illness and no headache.

Examination made after her admission to the Hospital gave the following results. The patient was lying in bed with a general appearance of great exhaustion. She was markedly emaciated. Her face was expressionless. Her eyelids drooped about half way over the pupils. This drooping is said to be variable, much worse some days than others. There was no palsy of the extraocular muscles and the pupils reacted to light and in accommodation. There was slight nystagmus. There was no apparent weakness in the masseter or temporal muscles and sensation to touch and pinpoint on the face was normal. She could not wrinkle the forehead but could corrugate the eyebrows slightly. The eyelids could not be closed completely and could not be held closed. She could draw back both corners of the mouth slightly but she could not whistle nor spit. She said that she felt a drooping of the lower lip and saliva occasionally drooled from the mouth. There was no impairment of hearing but bone conduction was lowered on both sides. The pharyngeal wall was anesthetic and the soft palate did not rise in phonation. There was no paralysis of the vocal cords (Dr. R. B. Canfield). The tongue could only be protruded slightly beyond the teeth and had a peculiar appearance in that the tip of the tongue was narrow and this narrowing extended about an inch to an apparent constriction about the tongue. There was no longitudinal growing as ordinarily seen in lingual atrophy and when the tongue was grasped with the fingers and pulled forward the constriction disappeared. There was no paralysis of the neck nor extremities and no sensory disturbances but the patient was so weak that she could not sit up nor hold up her head without support. There was no incontinence of urine or feces. There was marked general emaciation. The tendon reflexes were normal in the upper and lower extremities and there was no Babinski reflex. Mentally, she was perfectly clear and showed no retardation of thought. Articulation was much impaired; speech was slurring, typically bulbar and almost unintelligible. She had to be tube fed. The electric reactions in the facial muscles and in the tongue were normal both to the faradic and galvanic current. After tetanising the tongue about one minute with the rapidly interrupted faradic current, the irritability diminished but was rapidly recovered by a few seconds rest, (myasthenic reaction). Repeated contractions by the kathode of the galvanic current (100 contractions at one second intervals) caused no change in the amount or character of the contraction in the muscles of the face or tongue. Her heart and lungs were apparently normal. She frequently had epigastric distress after being fed and sometimes vomited. Her bowels were constipated. The temperature was normal. Pulse rate varied from 90 to 160. The changes in the pulse rate were sudden and not explained by any change in temperature. The attacks of tachycardia would last from twelve to twenty-four hours and were accompanied by the increased respiratory rate. Respiration was from 20 to 40 per minute. The urine showed no albumin nor casts and no sugar. The blood count gave 3,950,000 red blood cells, 12,950 white blood cells, and hemoglobin, 78 per cent. Miescher method. Differential leucocytes count: neutrophilic polynuclears, 81%; eosinophiles, 1%; degenerates, 6%; transitionals, 5%; large lymphocytes, 7%; small lympho-

cytes, 6% (patient menstruating). The Wassermann reaction on the blood was negative. The lumbar puncture showed the spinal fluid to be clear and colorless. The pressure was about normal. Only one lymphocyte was found in 5 cubic millimeters. The Nonne-Apelt reaction phase I, was negative; phase II, negative. The reducing substance was present in about normal amount. The Wassermann reaction on the spinal fluid was negative. The gynecologic examination (Dr. Reuben Peterson) showed retroversion of the uterus and pelvic adhesions. The ophthalmologic report (Dr. Walter R. Parker) was—"Retained nerve fibers, more marked in the left than in the right eye. Slight arterio-venous compression."

It is necessary to take into consideration a number of conditions in diagnosing a case like this but most of them are excluded easily. Post-diphtheritic palsy and pseudo bulbar palsy, due to bilateral cerebral lesions, are readily excluded by the history, and the same is true of so-called apoplectic bulbar palsy. The facio-scapulo-humeral type of muscular dystrophy gives a somewhat similar appearance to the face but does not cause difficulty in swallowing. Syringo-bulbia and brain tumor pressing on the medulla might give rise to the bulbar symptoms but the other signs of these affections are absent. Syphilitic disease of the brain might be thought of because of the history of a still birth and the reduction in bone conduction. However, there were no other signs of syphilis.

There are two types of bulbar palsy that are progressive. In the first of these atrophic changes are pronounced, the affected muscles show the electrical reactions of degeneration and the ocular muscles are not involved. This type occurs late in life, as a rule in the fifth and sixth decennium. A second type is the asthenic and myasthenic type. It occurs in younger individuals; there is usually ptosis, no marked atrophy and the electrical reactions are not those of degeneration but are the so-called myasthenic type. In the first type distinct pathologic changes are found in the medullary nuclei; in the myasthenic type such changes are not usually found. Dr. Kuh has recorded a typical case of this kind in which thromboses were present in the medulla. The prognosis is unfavorable in both types. Oppenheim records a fatal termination in twenty-six out of twenty-eight cases of the myasthenic type but it is quite possible for pronounced remissions to occur.

The etiology of this condition is not determined. It would seem as though congenital tendencies might play a part. In many of the reported cases anatomic peculiarities are noted —extra fingers or toes, web fingers, et cetera. In this case the retained nerve fibers are a peculiarity of the same order. Persistent thymus and thymus tumors are frequently found at autopsy in these cases. Autotoxemias, chronic infections and tumor toxins have been regarded as etiologic factors.

REPORT OF A CASE OF RELAPSING FEVER.

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History.—The patient, Dr. C. P. age 37, was admitted to the University Hospital, January 19, 1914, complaining of headache, severe backache and a feeling of malaise. The paternal grandfather died of tuberculosis and twenty-five years ago his father died of pulmonary tuberculosis at the age of 48. The patient has had the usual children's diseases. For the past two years he has lived in Augusta, Georgia. He has never had malaria.

Present Illness.—The present illness began January 15, 1914 with malaise but he was not sick enough to stop work. Two days later he complained of "feeling miserable" and of headache over the eyes; also at this time he had an aching pain in the lumbar region. January 18, patient became much worse, taking to his bed with a poor appetite, complaining of feeling dizzy when on his feet. His temperature at this time was 101°. He had no shaking chills, sore throat, coryza, sweats nor vomiting; the bowels were regular and there was no urinary trouble.

Examination.—On examination the temperature was 102.4°, pulse 104, respirations 22. The patient was underweight and poorly nourished, somewhat anemic. There was no general glandular enlargement. Examination of the chest disclosed slight impairment to percussion over the right apex with harsh vesicular breathing and definite crackling râles, which were persistent after coughing. The heart was negative. A few crackling râles were heard over the right apex behind. The spleen was not palpable and the liver was apparently not enlarged. The urine and the stools were negative.

Course.—The temperature dropped to normal on the evening of the day of entrance and remained normal until discharge. This occurred by crisis, dropping from 101° to 98.6° in four hours. An examination of the blood showed 4,600,000 red cells, 3,000 white cells and 85% hemoglobin. Differential count; polymorphonuclear cells 62%, large lymphocytes 30%, small lymphocytes 6%, transitionals 2%; one normoblast and 8% degenerated large lymphocytes were seen. While making the differential count and looking for malarial parasites, one characteristic spirillum was found.

Diagnosis.—A diagnosis of relapsing fever was made and the patient given three tenths of a gram of neosalvarsan that afternoon.

Relapse.—The patient remained well up to February 1st., when he began to have a feeling of malaise and headache. He kept about until February 8th., when his headache became so severe as to make him take to his bed. He noticed pain in the lumbar region and considerable soreness in different parts of the body, including his testes. There was no definite chill. His temperature taken February 4th., was 99°. On February 5th. he had a temperature of 100° and on the 6th a temperature of 101°. From the 4th of February he ran a continuous, irregular temperature and on Monday, February 9th, he entered the Dermatologic clinic for another treatment. His temperature fell by crisis that same night. The spirillum was looked for in the beginning of his last illness on numerous occasions by Dr. Novy and his assistants. He was so sick on February 8th, that examinations on this day were omitted. A smear was taken on February 9th, but no spirilla were seen. I am sorry that the patient did not notify me of this recurrence, as he promised to do before he left the Hospital.

It is well known that the relapsing fever of America shows very few organisms in the circulating blood. I wish I had had an opportunity of searching for the organisms by centrifuging ten cubic centimeters of this patient's blood after laking the red blood cells. This method has worked very well in isolating tubercle bacilli and the embryos of trichinae.

The patient had been working in the bacteriological laboratory of the University of Michigan, although not directly with the spirillum of relapsing fever, but claims to have been bitten by rats inoculated with this organism. There is some evidence to show that the disease can be conveyed by contagion, such as clothing or the handling of the bodies of patients who have died of the disease. It has been definitely proven that the disease is transmitted by ticks, head lice, and possibly the bed bug. In 1905, Carlisle of the Bellevue Hospital reported two cases of relapsing fever, the second the result of the bite of an infected monkey inoculated with the organisms from the first case. S. T. Darling in the *Archives of Internal Medicine,* 1909, reports five cases of relapsing fever inoculations occurring either through the skin or due to the bites from infected monkeys.

Relapsing fever is a specific infectious disease frequently occurring in epidemics. An attack is characterized by a fever of about six days duration, followed by a remission of the same period, then another attack of fever, occasionally a third attack, rarely a fourth or fifth. The disease is self limited, rarely fatal in itself, death usually being due to complications, of which pneumonia is the most frequent. The small mortality is found in the debilitated and aged. The incubation period is very variable, usually from five to fourteen days. There are very few prodromal symptoms, generally a feeling of malaise, the disease setting in abruptly, usually with a chill, followed by a rapid rise of temperature, rapid pulse, accompanied by continued and severe headache, dizziness and pain in the back. The general condition grows rapidly worse, forcing the patient to bed on about the second day. The appetite is lost, other gastric symptoms varying considerably. The headache continues with marked insomnia. There is usually enlargement of the spleen and liver and frequently a polymorphonuclear leucocytosis. Often on the sixth day there is a sudden fall of fever, by crisis, which usually occurs at night. About thirty or forty per cent. of the patients have only one attack, but during a relapse the organisms may again be isolated from the blood. Not infrequently the second attack is worse than the first.

The specific cause of the disease is due to an organism described by Obermeier of Berlin in the year 1873. The parasite is a delicate, colorless, spirally-twisted organism, resembling a fine thread of fibrin, about ten to fifteen microns in length. When found in the blood it is easily seen moving about among the red blood corpuscles, apparently never quiet, progressing forward or backward. No definite structure has been made out, although in some instances, a granular or beaded appearance has been noted. This was observed in our organism which was treated with Hasting's stain. The number of organisms found from day to day varies greatly. As a rule there are few early in the attack, but they gradually increase in number, reaching the maximum shortly before the crisis, when they decrease rapidly and may completely disappear. The cause of the disappearance of the organisms is unknown. The disease can be conveyed to another individual by inoculation of the blood during a paroxysm. Certain insects, such as bedbugs, may suck the spirilla and in this way produce the disease by biting. Dr. Novy has suggested that there are probably four forms of relapsing fever in man. There are no characteristic pathologic findings in patients dead of the disease.

Intravenous injections of salvarsan or neosalvarsan in moderate doses, usually abort the disease or prevent further attacks.

DISCUSSION.

DR. FREDERICK G. NOVY: I am very glad to discuss this unusual case. The question of how these infections occur in the laboratories is an interesting one. The transmission by insects, the natural mode of infection, is practically excluded in these laboratory accidents, unless the work actually involves the study of such parasites. In some instances there

is no evidence at all of a bite caused by an experimental animal, such as the monkey or rat. There may even be no evidence of an injury, such as a scratch or cut which would facilitate the entrance of the specific organism. Under these circumstances one is obliged to seek for an explanation of such infection in the known fact that spirilla can penetrate through the unbroken mucous membrane and even through the unbroken skin. A minute drop of infected blood brought into contact, in some way, with the mucous membrane of the mouth or nose, or with the conjunctiva, is sufficient to bring about an infection. As a matter of fact this is one stage in the natural mode or transmission of the disease.

As regards the natural mode of transmission, I would like to emphasize one point already mentioned, and that is that certain insects are the natural means for the spread of the disease. We have two good illustrations of this fact. The tick fever of equatorial Africa is produced entirely by the bite of a tick, the *Ornithodorus moubata*. In Northern Africa and in Europe this tick does not exist and hence some other intermediate host must be sought for. The work carried on in Eastern Europe has not helped materially to clear up this point. In Northern Africa, more especially Tunis, the local relapsing fever has been shown conclusively to be spread through the agency of the body louse. Nicolle and his co-workers, in Tunis, demonstrated first that the mere lines of lice which had fed on infected animals did not produce the disease in man or monkeys. In other words, the bite itself was inoffensive although there was every reason to believe that the louse was the means of transmission. They found that the spirilla which were sucked up with the blood by the louse, soon disappear from the intestine and cannot be detected anywhere for a period of 8 to 19 days. The spirilla then appear, not in the gut, but in the lacunar cavity. Since infection of man does not follow the mere bite of such infected insects; nor result from fecal deposition on or about the wound, in the process of feeding by the insect, it became apparent that infection could only occur through the crushing of the biting insect and the consequent liberation of the spirilla. These may then come into contact with the wound; they may be carried by the finger tips to the eye, mouth, or nose, and thus give rise to the disease. These facts have been ascertained by direct experiments upon the laboratory staff.

A point that I want also to call attention to is the extremely beneficial results obtained with salvarsan. If there is any thing in which salvarsan is good, it is in relapsing fever. In this particular case there was a relapse, following the first injection. An attack of the disease, or a relapse, can be jugulated by an injection of salvarsan, if given at the onset of the symptoms.

A CASE OF KORSSAKOW'S PSYCHOSIS COMPLICATED BY CEREBRO-SPINAL SYPHILIS.

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Mr. M. was found on Sunday morning December 9, 1913, in an unconscious condition in the back room of a downtown saloon. At first his friends thought that he was drunk as usual but this idea was abandoned when his condition did not improve. During the afternoon he had a series of convulsions and his people became alarmed. Being unable to arouse him out of his stupor, it was finally deemed advisable to send him to the University Hospital. He was admitted to the Medical clinic at nine in the evening. At that time he had a rectal temperature of 104°; he was stuporous and unresponsive. Shortly after admission he vomited. The vomitus was non-specific; however, to make sure, his stomach was thoroughly washed.

The history of the case was meager and one could, therefore, only speculate as to the probable trouble. Was he poisoned as his parents suspected? Did he have uremia, diabetic coma, apoplexy, epileptic stupor, cerebral syphilis or beginning delirium tremens? Any of these conditions might well produce a stupor with convulsive seizures. Inasmuch as there was no difference in the muscular tonus of the two sides, no sterterous breathing, and the temperature was not normal or subnormal, apoplexy was practically ruled out. During the following morning, he had a series of six convulsions which were epileptiform in type. His temperature was 103.6°, his breathing rapid. On the whole he was quiet. He did not speak, but when touched, he would look around. The examination of the heart, lungs and abdomen was negative. His urine contained a heavy trace of albumin and numerous casts, but no sugar, diacetic acid or acetone. Since he really was not comatose, and showed no evidence of air hunger, diabetic coma was improbable. The absence of diacetic acid and acetone in the urine ruled out that condition definitely. Uremia was not so easily disposed of; for that disease may commence suddenly, often with a loss of consciousness and epileptiform attacks. Usually the patients are confused, unclear and delirious, though sometimes they may be sullen and apathetic. But since the urine showed only a trace of albumin and was not loaded with casts, it was not thought necessary to make a urea determination of the blood.

The microscopic examination of the blood added still another possible diagnosis. The examination made by Dr. H. Schmidt showed 3,400,000 reds, 24,000 whites, mostly polymorphonuclear and a hemoglobin of 83% Miescher. The study of stained blood smears revealed marked aniso-cytosis, considerable polychromasia and large numbers of basophilic stipple cells. No nucleated reds were seen. In other words the blood picture strikingly resembled that of lead poisoning. This was, indeed, interesting, for plumbism might well produce the entire symptom complex. The mental and cerebral symptoms in lead poisoning, classed under the head of encephalopathia saturnina, are usually hemianopsia, delirium, coma and convulsions, mostly of the type of general-

ized epilepsy. Though he had occasionally assisted in the painting of barns, it was learned that he had not done any work of that kind since June. Examination showed neither anemia, wrist drop nor a lead line on the gums. Subsequent chemical analysis did not reveal even a trace of lead in the urine and so the hope of a striking diagnosis vanished.

During the afternoon he became so restless and apprehensive that it was difficult to restrain him in bed. Fearing delirium tremens, he was committed to the Psychopathic Hospital on an emergency order. Soon after his transference. he became quieter and took liquid nourishment in large quantities. With the aid of a dram of paraldehyde, he slept six hours the first night. On the following morning his bowels were exceedingly loose. He co-operated to some extent with the attendant. He looked apathetic and sleepy. To most questions, he answered with absolute indifference "Oh, I don't know." Two days later his temperature again went up to 103°, the breath sounds over the right side of the chest were harsh and the expansion somewhat decreased. A central pneumonia was suspected; however, the temperature did not stay up long and the breathing soon became easier. During the next three days, he improved considerably. He looked and felt better and answered questions more promptly. He thought it was Thursday, August, 1999, and that he was over Myer's saloon in Ann Arbor. He asked for Miss S. and said that he had seen her several times that morning. He gave Washington as the president of the United States and said that he had been elected by the progressives. When questioned later regarding his drinking habits, he admitted that he had indulged heavily for the last ten years. Usually he consumed from five to six bottles of beer a day. About once a month, he went on a drunk for two or three days. On these occasions he mixed his drinks. This last time he got in with some cronies from Jackson and they were together Thursday and Friday, consuming half a barrel of beer and several quarts of whiskey. He remembered being at Myer's beer-house after they had left, but for the time that elapsed between Friday and Thursday morning he is amnesic.

Judging from the account obtained from his mother, it is evident that he comes from a family of low type with a history of alcoholism and pauperism. The maternal grandfather was a heavy whiskey drinker and an occupant of the Washtenaw county house for years. Two brothers of the mother, the maternal cousins and one of the patient's brothers are heavy drinkers. The patient is said to have developed normally. It is not known how much schooling he had. He stopped somewhere around twelve because of his unwillingness to continue. He worked as a farmhand and later as a common laborer. He commenced drinking at about nineteen, but it was only during the last five years that he has drunk to excess. He takes something every day and according to the mother he is intoxicated four or five times a week. Without liquor he is extremely nervous and practically helpless. During the last year, he has done odd jobs, helping around saloons, painting a barn occasionally and collecting junk. There is no history of epilepsy in his own past life. Epileptic stupor was, therefore, unlikely and in view of the subsequent developments, entirely out of the question.

He is a man thirty-nine years of age. Examination revealed an enlarged liver, but normal blood pressure and normal vessels. There is a smooth scar back of the corona, which he said resulted from a hard sore four years ago. The left pupil is a little larger than the right. Both react fairly well to direct and consensual light stimuli and in accommodation. The extraocular movements are fairly well performed. The acuteness of his taste is diminished. He shows considerable hyperalgesia and hyperesthesia. He is sensitive over the nerve trunks of the extremities. The left knee jerk is present and about normal. The right knee jerk and the left Achilles jerks were absent even on re-enforcement. There was a questionable Babinski on the right. There were, therefore, numerous polyneuritic disturbances which might well be produced by chronic alcoholism. But why did he not clear up after his acute delirious episode? Was he passing into Korssakow's psychosis? This condition might well be expected in view of his heavy drinking. Twenty-five per cent. of the cases of Korssakow's psychsis according to Kraepelin do begin with an acute delirium, sometimes with epileptiform attacks. Instead of clearing up within a few days, they pass over into a chronic state showing apathy, irritability, marked memory defect, confabulation and polyneuritic disturbances.

Re-examination of the urine December 11, 1913 showed a trace of albumin and numerous granular casts. The blood count made on the same day showed 4,200,000 reds and 24,000 whites. Five days later the white cell count had fallen to 20,000. On neither occasion could any stipple cells be found in the smears. The cerebrospinal fluid examined on December 16 contained 38 cells per cubic millimeter; the globulin test was positive in a dilution of 1 to 10; Nissl-Esbach 3.0. The Wassermann was four plus positive both on the blood and the spinal fluid. Here was another complicating factor. Was his attack due to a combination of alcoholism with general paralysis? Was that the reason he did not clear up from his acute delirium? But his infection was only four years ago and the

peculiar polyneuritic disturbances could hardly be produced by general paralysis.

For two weeks after admission to the Psychopathic Hospital he continued to be disoriented, always thinking he was over a saloon and that he had been there about four days. He was unable to return numbers of five digits and when short stories were read to him, he could not repeat them. He was unable to detect the most evident absurdities. He had some difficulty with the usual test phrases. Even in writing his name he made numerous mistakes, such as reduplications and transpositions. He also showed a slight tremor. He could not write Ann Arbor or the word saloon. In writing the abcs he only got as far as b and ended with *or*, still thinking that the physician wanted him to write Ann Arbor.

On December 20th, early in the morning, he had five severe epileptiform convulsions, each lasting about four minutes. He was unconscious for over two hours, but after that he was as clear as usual. By the third of January, 1914, he had gained five pounds in weight and as a consequence he had improved considerably in appearance. Though oriented, he still was unable to repeat short stories when they were read to him, but when a story was told him in simple slang fashion, he gave most of the details fairly accurately. There was no tendency to confabulation. He did very poorly in writing the alphabet. He rarely got beyond d or f and then often repeated many of the letters given previously. He excused himself by saying he never went to school more than three terms. In writing his name, he still showed a slight tremor and added an extra letter. Re-examination January 10th showed that the reflexes which had been absent had returned, though they were still much diminished in comparison with their fellows. His station and gait were normal and there was not even a questionable Babinski. Though he could add and subtract successive sevens correctly, he could not figure out what year it was seven years ago. A second lumbar puncture made January 3rd showed 32 cells per cubic millimeter, globulin positive in dilution of 1-5, Nissl-Esbach 1.5 and again a four plus positive Wassermann. Both the cell count and the globulin were, therefore, less than on the first examination.

During the last month he has continued dull and uninterested. Whenever he cannot answer questions, he becomes irritable and refuses to co-operate further. He knows the name of only one of the physicians. Even when speaking of his friends downtown, he rarely is able to give their names. He is correctly oriented and knows approximately how long he has been at the Hospital. He has no conception of the seriousness of his condition before coming to the Hospital; he knows no more about it than what his father told him. His perception is better on the whole and he can figure out what year it was seven or thirteen years ago. There is now no noticeable articulatory defect in his spontaneous speech. The urine and blood are negative. A third lumbar puncture made on February 7th showed a cell count of seven, Nissl-Esbach 1.2 and globulin positive in equal quantities but negative in dilution of 1 to 5. The Wassermann is still four plus on the blood and the spinal fluid. The cell count, globulin, and Nissl-Esbach have, therefore, come down to practically normal. These findings make the presence of general paralysis very improbable.

According to the reports of Assmann (2), Nonne and Holzmann (3), Betz (4) and Peyton Rous (5), the cell count, the globulin and albumin are normal in cases of chronic alcoholism and Korssakow's psychosis. This agrees with the fluid findings of the four cases of chronic alcoholism (two of which were cases of Korssakow's) that were punctured at the Psychopathic Hospital. In two cases the Nissl-Esbach was slightly increased. But inasmuch as this patient has a persistent Wassermann on the spinal fluid, cerebrospinal syphilis cannot be excluded. Since there was a progressive improvement in the cytologic and chemical findings of the cerebrospinal fluid, one might infer that a latent luetic process had become temporarily active by reason of the alcoholism.

We have then a man who has been a heavy drinker for years, taken down suddenly with epileptiform convulsions, passing over into a stuporous state and then into an atypical delirium. This gradually cleared up, leaving him dull, apathetic, and with polyneuritic disturbances, marked defect in his memory and discrimination, but showing no tendency to confabulation.

In view of these findings, the diagnosis of Korssakow's psychosis combined with cerebrospinal syphilis seems wararnted.

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2. Assman: *Deutsch. Ztschr. f. Nervenh.,* XL, 131.
3. Nonne and Holzmann: *Deutsch. Ztschr. f. Nervenh.,* XXXVII, 195.
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5. Peyton Rous: *Am. Jour. Med. Sc.,* CXXXIII, 571.

DISCUSSION.

Dr. H. B. Schmidt: This patient entered the Medical clinic as an emergency case. An examination of the blood disclosed a considerable amount of stippling of the red blood corpuscles. As there was practically no anemia, lead poisoning was considered as a probable cause of his coma and convulsions. There was no lead line present, but as we know that in either acute or chronic intoxication from lead, especially in alcoholics, delirium, delusions

and coma may be present, we still considered lead encephalopathy as a diagnosis. A sample of his urine was examined by Dr. Vaughan on two occasions and found negative for lead.

He remained in the Medical clinic only a short time, about thirty-six hours, and re-examination of the blood with Unna's stain showed that the stippling had almost completely disappeared and was not typical of lead poisoning, in that the granules did not take the red stain. This is very important in differentiating the stippling of the red cells seen occasionally in a normal blood from that seen in severe amemias and lead poisoning.

AN ESTIMATE OF THE VALUE OF THE WASSERMANN REACTION TO THE GENERAL PRACTITIONER.

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The last decade in medicine has seen an enormous growth in knowledge concerning syphilis. Indeed, it may be said that in no other field of medicine, either clinical or experimental, has there been greater progress made than in the study of syphilis. The discovery in 1905 by Schaudinn and Hauffman, of the infecting organism, and of the complement fixation test of Wassermann were forerunners of an epoch of research which has resulted in a great accession of knowledge to the practitioner of medicine and incalculable benefit to mankind.

It was my good fortune to have been one of the first American students of the complement fixation test, to have performed this work under one of Germany's foremost serologists. It has fallen to my lot of late on several occasions to defend this wonderful laboratory test before early sceptical audiences. I have recently expressed myself as favoring, for the protection of the hospital staff, a routine, compelling all entrants into hospitals to submit to the Wassermann test before their admission. I mention this positive stand which I have taken to offset any idea which may arise from the theme of my paper this evening. I wish to point out herein that notwithstanding the enormous gain which the complement fixation test has brought to clinical and experimental medicine, its wide and indiscriminate use has not been entirely without disadvantage to the practicing physician.

A proper estimate of the value of the Wassermann reaction to the practicing physician must take into account, first, the limitations of the reaction itself, and, second, its judicious application. With regard to the first factor, it must be admitted at the outset that there is a great variability in the technic of the reaction as it is carried out. There is even a daily difference in the efficiency of the various reagents. Secondly, in a reaction so complicated and so delicate, there are constant sources of error cropping out, and lastly, the question of the personal equation enters into the interpretation of the test. For example, in a doubtful case, what to one observer's eye and judgment is read as a partial hemolysis, may be interpreted as doubtful by him; a second observer might read the same test as faintly positive and a third might regard it as negative. It has been my custom in important cases to divide the specimens and to compare the readings of two different observers of the clinical findings and thus place a check, as it were, on the result of the test.

First and of paramount importance, the practicing physician who wishes to employ the Wassermann reaction must know the ability of the laboratory technician who is to carry out the test. Within the past few years, numberless advertising laboratories and even druggists have placed their resources at the command of the practitioner for the performance of the complement fixation test. I am satisfied that for the most part their work is entirely unreliable.

A second point of no less importance has to do with the limitations of the test itself. Far too often is the fact forgotten that in the first stages of the disease, and practically during the entire period of the development of the chancre, the test is uniformly negative. A test taken at this time is, therefore, useless. It is regrettable that a negative outcome at this period is still interpreted as negating syphilis, to the chagrin of the physician at a later date, and occasionally to the irreparable damage of his patient.

During the secondary period, the reaction may be said to be more uniformly positive, and probably the fewest errors are made during this period. But even here, a negative outcome may trap the unwary. The most malignant, precocious types of syphilis are occasionally characterized by a negative reaction. During the past year I have seen two such cases—in the first a profuse follicular, and in the second a rupial, syphilid. Both were frankly negative in the blood. In the tertiary stage of syphilis, according to different observers, from fifteen to thirty per cent. of all cases react negatively. Taking the lowest estimate, the physician who places his sole reliance on the outcome of the test, takes a fifteen per cent. chance of being wrong. In hereditary syphilis with manifold lesions, practically all cases react positively, but in the latent stage, a negative reaction is not infrequent, and it often occurs that children whose blood at birth is negative, develop syphilis within a few weeks after the test has been taken.

Of great value to the general practitioner is the employment of the test upon wet nurses. It goes without saying that no woman should

be engaged for a healthy infant who has not first submitted to the Wassermann test.

A not uncommon error where entire reliance is placed upon the outcome of the test is found in the fact that the patient may have a latent syphilitic infection which is in no way connected with the condition for which he requires active treatment. In particular does the diagnosis of abdominal and thoracic neoplasms thus suffer from a lack of clinical study. The presence of a positive reaction in such cases is, it is true, evidence of a syphilitic infection, but only presumptive evidence that the condition in question is due to syphilis. In cases such as this, in fact in all obscure cases, the result of the test should be carefully weighed against the clinical features of the disease.

The greatest importance, however, attaches to the value of the test as a guide to the efficiency of treatment. A decade ago and before, careful medical men followed the teaching of a great syphilologist who taught that syphilis must be treated at least two years, and better, three. This was a purely arbitrary rule based upon a vast experience which showed that if treatment were carried out energetically for this period of time, patients remained well, had no late lesions, and could safely marry and be the progenitors of healthy offspring.

We now know that some syphilitics get well within a year; that others require two or three or more years to cure; and that some, indeed, never get well. It was an early observation in the history of the complement fixation test that a positive reaction tended to become negative under treatment, if the latter were efficient and persisted in. Frequent reactions, therefore, taken during the periods of repose in treatment serve as an excellent guide as pointing to the efficiency of our treatment. Here again, however, a word of caution. A negative test taken during the time that the patient is under treatment is of no significance, and no test should be made until at least from four to six weeks following cessation of all treatment. During the past week, I was consulted by a man who came to me, as he said, for a blood test. He had contracted syphilis last July. A blood test taken one week after an intravenous injection of salvarsan, and at a time when he was taking mercury, was said to be negative, and his physician pronounced him cured. There was no need for a second blood test. The examination revealed recurrent lesions in the mouth and a papular syphilid of the chin.

In general, it may be said that a negative reaction gains in value and significance with each succeeding negative test, and a cure should never be pronounced until the reaction has remained negative on several successive trials.

While it is undeniably a fact that a persistent positive Wassermann means a latent infection, it is nevertheless also a fact that occasionally patients in a latent stage of syphilis will have a positive Wassermann reaction which remains so notwithstanding all forms of treatment. Such cases not infrequently remain in perfect health. They marry with impunity and become parents of healthy children. Such cases occur particularly in those in whom treatment is begun late in the course of the disease. While it is a fact that a positive Wassermann in the active and early stages of the disease means the occurrence in the blood of antibodies or immune substances which are called forth by the presence of the infection itself, yet it appears not unlikely that in these cases with persistent Wassermann reactions which resist all forms of energetic treatment and yet remain perfectly well, the presence of complement binding substances is due to a chronic change in the blood not necessarily activated by living spirochaete. Personally, I have seen a number of such cases in which matrimony or the resumption of marital relations has resulted in perfect children and in nontransmission of the infection to the mate.

There is, as you all know, in a neighboring state, a law which requires all candidates for matrimony to submit to a Wassermann test. Although the wisdom of such a law is unquestionable, its application at the present time is difficult. While a step in the right direction, it is, if carried out on the blood alone, really a half-way measure. To give a man or woman a clean bill of health, not only should a test be made on the blood but also upon the spinal fluid. A certain percentage of cases of cerebrospinal syphilis, active and latent, is negative in the blood and positive in the spinal fluid. Obviously, permission to marry should be withheld in such cases as these. Moreover, the ends of such a law may be defeated by the fact that the reaction may be temporarily inhibited by active treatment coincident with the time of the taking of the test. A careful physical examination at the same time will usually offset this possible error. It is, perhaps, a matter of a short time when all states will have similar statutes on their books, and for uniformity of results, it will then be necessary to establish state laboratories of serology.

I wish now to turn to the second axiom of my theme—the judicious application of the test. While it is true that the Wassermann test has cleared up many hitherto obscure conditions and placed them on a syphilitic basis, it is nevertheless also true that syphilis in all its forms was recognized before the days of laboratory aids. The statement that the indiscriminate use of this test in practice is making for poor clinicians, is not, I think, too broad. We are losing in medicine that fine type of mind which made for keen observation and deductive reasoning.

There is no cutaneous nor mucous membrane syphilid which requires a Wassermann test for its diagnosis. The careful surgeon can and should be able to differentiate gumma from sarcoma or tuberculosis of bone. A discriminating internist of the older school required no Wassermann test to diagnose syphilitic cirrhosis or early syphilitic anemia. The countless manifestations of syphilis are not difficult of clinical recognition if care be given to their study.

The teaching of syphilis in our schools should be, I believe, toward the development of that faculty of keen observation and deductive analysis which characterized the clinician of an older day. If more time were expended in developing such faculties, we would then be equipping students who were capable of recognizing a chancre without a dark-field, and who would reflect twice before operating on gummatous lesions.

In conclusion, permit me to advise the general practitioner to make use of the Wassermann test, but to use it very judiciously; to be sure when using it of the laboratory technician's ability; to avoid its frequent use as a diagnostic aid by acquiring through study of syphilitic lesions and manifestations the diagnostic touch and eye which makes the unravelling of disease processes ever a new and fascinating study.

DISCUSSION.

Dr. William A. Pusey, Chicago: I am glad to hear Dr. Wile discuss the Wassermann reaction and I am surely in accord with most of what he says. There is one point that Dr. Wile made which should be especially emphasized—that the Wassermann is not always positive in the presence of active syphilis. Some syphilographers insist that they get a positive Wassermann in all active syphilis. If there is a chance of twenty per cent. negative reactions in the presence of active syphilis, one is up against the possibility of making a great many mistakes. I am reminded of a case I saw a year ago—a man with a perfectly clear ulcerating syphilid of the leg. He had a negative Wassermann and, because of this, his doctor excluded syphilis. I said to the man, "This is syphilis." "It is not syphilis," he said. "I wish it *were* syphilis—I might get well if it were I had a negative Wassermann. I haven't had syphilis for twenty years."

I do not agree with Dr. Wile in his statement that repeated negative Wassermanns indicate that the patient is well of syphilis. In McIntosh and Power's book there is a discussion as to when a patient can be pronounced cured of syphilis. "Only after repeated negative Wassermanns extending from one to two years, and often conscientious syphilologists can only say so after twenty years." I should say that conscientious syphilologists could *never* be sure that a patient is absolutely well of syphilis. Regardless of the disappearance of symptoms, the syphilitic infection may remain and reappear years later.

Dr. Wile says that no patient with a positive Wassermann is entitled to marry. As a matter of fact, for many years I have assumed that after five years of cessation of symptoms of syphilis, syphilitics could marry. Jonathan Hutchinson used to let most of his syphilitics marry after two years. Fourner allowed his to marry after five years. It is a rule, however, that may be followed by disastrous results. This means that a vast number of men marry after five years who have a positive Wassermann, for a vast number of syphilitics remain positive intermittently for life. Some of these patients marry and raise healthy families. In the face of that fact, however, I think that a man is not entitled to marry after five years with a positive Wassermann. We cannot give anybody absolute assurance of having healthy children, no matter who he is. In the present condition of our knowledge, I think we are not warranted in taking that hard and fast stand with regard to the Wassermann.

Dr. Wile (closing the discussion): Dr. Pusey and I do not differ very much after all with regard to the ability of patients with a permanent positive Wassermann to marry and have healthy children. That is a point which I emphasized in my paper and I agree with Dr. Pusey that, while we cannot assure them of healthy offspring, the fact, remains in the absence of all symptoms for many, many years that such patients remain well. I do believe, however, that a negative Wassermann gains in value with each successive test and that there comes a time when we should take upon ourselves the responsibility of saying that the patient is well. This, therefore, must remain a difference of opinion between us.

TRANSACTIONS
OF THE
CLINICAL SOCIETY
OF THE
UNIVERSITY OF MICHIGAN

STATED MEETING, MARCH 11, 1914

THE PRESIDENT, R. BISHOP CANFIELD, M.D., IN THE CHAIR
REPORTED BY REUBEN PETERSON, M.D., SECRETARY

Reading of Papers

A DIAGRAM OF THE HEART CYCLE, PICTURING THE CHANGES OF FORM OF THE AURICLES, VENTRICLES, CARDIOGRAM, AND VENOUS AND CAROTID PULSE CURVES.

WARREN PLIMPTON LOMBARD, M.D.

Professor of Physiology, University of Michigan.

The diagram which is here presented is brought before you, not because it contains any new facts, but in the hope that a picture of the series of phases through which the heart passes in the course of a normal cycle, and the synchronous changes in the form of the cardiogram, and the records of the venous and carotid pulse may serve as a basis for a discussion. Much of our knowledge of the action of the heart, and its relation to the circulation of the blood, has been in the past contributed by the scientific practitioner and it is probable that in the future we must look to the work of the clinical even more than of the physiologic laboratory for advance in this direction. Many of the points which are illustrated in the diagram are far from settled, and as divergent views cannot appear in a single scheme, it is necessary to present those which seem to have the strongest support and which fit into a harmonious whole. I know that there are many present who, through their daily study of the changes wrought in the action of the heart by disease, will be capable of suggesting important changes in the picture which is offered, and it is in the hope that such suggestions will be made that the diagram is brought before you.

The diagram assumes that a normal heart is beating at the rate of 75 per minute and that one complete cycle occupies eight tenths of a second. Each of the spaces enclosed by the unbroken vertical lines is o. i. second; and in the horizontal spaces, reading from above downward we see the duration of the systoles of the auricles and ventricles, and the period of diastasis; the time of occurrence of the heart sounds; the periods when the semilunar and the auriculoventricular valves are open; (the upper light band covering the period when the semilunar valves are open, and the lower light band showing when the auriculoventricular valves are open); the changes in the form of what may perhaps be regarded as a typical cardiogram; the waves of the venous pulse; two serial views of the changes of form of the auricles and ventricles of the right heart, the large arteries, and the position of the heart valves, (the upper series being given because it illustrates the action of the heart with respect to the associated waves of the venous pulse curve, and the lower because it pictures the relation of the heart to the pressure waves in the arteries); and, finally, at the bottom, a sphygmogram of the carotid pulse. Of course these schemes of the action of the heart are purely diagramatic. The ninth heart picture on the lower line would be a truer representation of the heart. In fact, to bring out the effects of action, great liberties have been taken; only two curtains of the tricuspid valve are shown; the pulmonary artery is made to lie in close contact with the right auricle, although as it winds around the aorta, it is the aorta which is most intimately related to the wall of the right auricle; the right ventricle is pictured as forming the apex of the heart, although in fact it is the tip of the left ventricle which is the apex. The horizontal lines beneath each of the series of hearts represent the chest wall. Allowance has been made for the postponement of the venous and carotid pulse curves, by shifting them a little to the left, so as to bring them into closer relation to the processes upon which they are supposed to depend.

I propose to take up each 0.1 second of the cycle in order, and to review the processes depicted as occurring during each successive period.

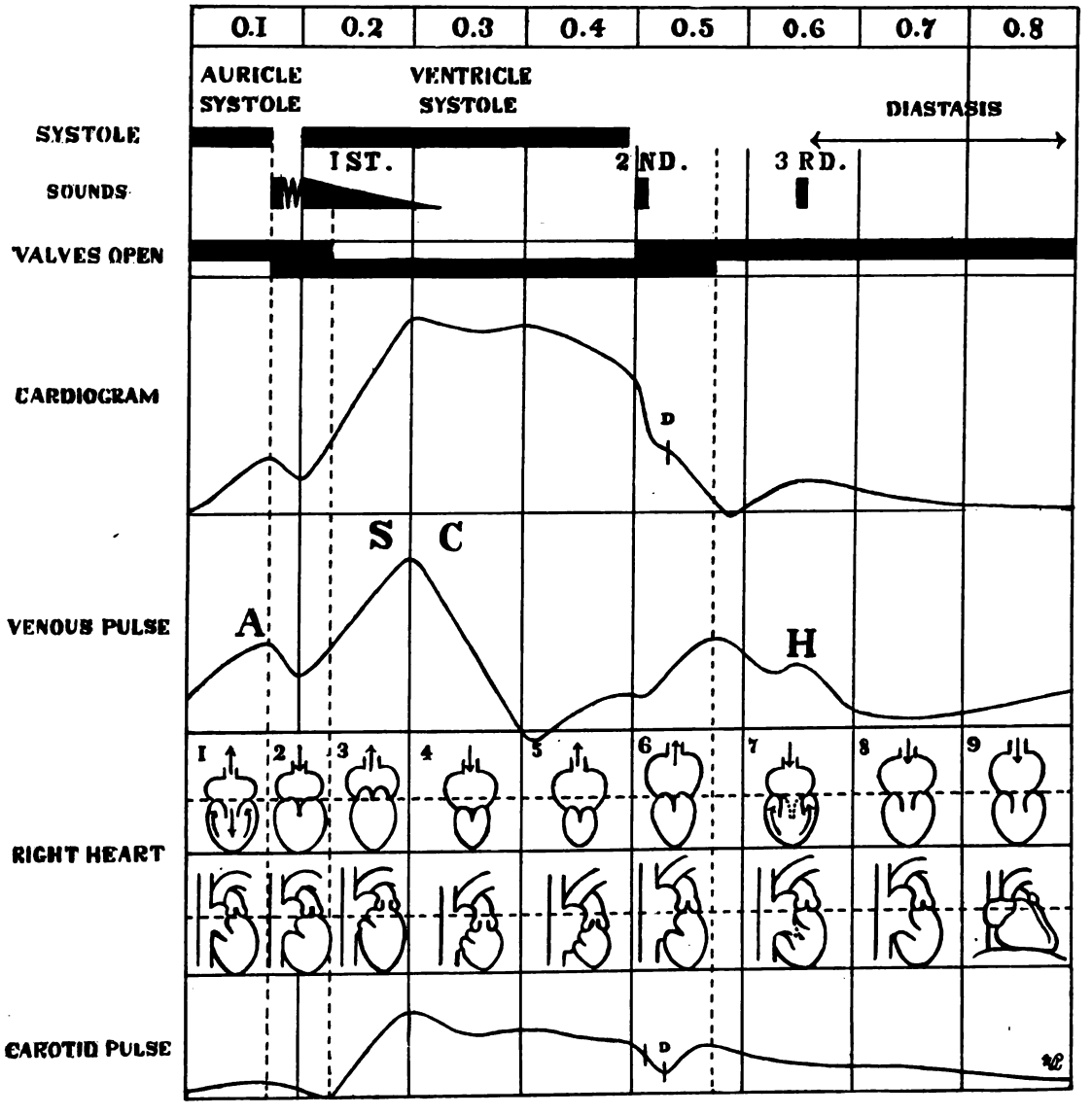
THE FIRST TENTH OF A SECOND.

VALVES. The semilunar valves are closed. The auriculoventricular valves are open at the start and are closed toward the end of the period, because of the brief, rapid injection of blood into the ventricles by the systole of the auricles, this being followed by an immediate relaxation of the auricle and an elastic recoil of the ventricular wall.

AURICLES. The auricles contract and complete the filling of the ventricles and then suddenly relax, (the relaxation is helped by the elastic recoil of the lung fibers which were stretched when the auricle contracted. This is especially true of the right auricle. Both auricles are, of course, affected by the continuous negative intrathoracic pressure).

VENTRICLES. The ventricles, already full, are suddenly slightly over-filled by the quick, contraction of the auricles. Pressure currents are working behind the valve curtains, and the elastic recoil of the ventricular walls closes the valves.

CARDIOGRAM. The suddenly distended ventricle presses on the wall of the chest during the systole of the auricle, and then suddenly



A diagram of the heart cycle, picturing the changes of form of the ventricles, cardiogram and venous and carotid pulse curves.

lessens its pressure, as the auricle relaxes. The cardiogram records the auricular systole.

VENOUS PULSE. The record shows the "first positive wave," a pressure wave, due to the sudden increase of tension in the auricle as it contracts and completes the filling of the ventricle; and "the first negative wave," a negative pressure wave, caused by the sudden relaxation of the auricle.

CAROTID PULSE. A very slight wave is often seen, corresponding to the contraction of the auricle. These changes originate at the root of the aorta, and are caused by the expansion and the elastic recoil of the wall of the ventricle, as a result of the injection of blood by the auricle.

THE PRESPHYGMIC PERIOD.

This period falls between the two dotted verticle lines, in the latter part of the first tenth of a second, and the first part of the second tenth of a second. It extends from the time that the auriculoventricular valves close, to the time that the semilunar valves open, that is, it is a period during which both sets of valves are closed.

VALVES. The first sound of the heart begins with the closure of the auriculoventricular valves, very early in the period, and the quality of the sound changes during the period, the valvular element merging into the sound waves thrown out by the cordae tendinae, and immediately after, by the muscle fiber of the walls of the ventricles, when they are suddenly put under tension.

AURICLES. The auricles suddenly enlarge at the very beginning of the period, so that the pressure falls below the ventricular.

VENTRICLES. The pressure falls suddenly for a brief period, as the auricles relax, and then begins to rise as the ventricles begin to contract, during the latter part of the period. As they contract, the ventricles harden; the apex is rotated forward, and to the right, so as to press more firmly on the wall of the chest; the ventricles begin to narrow laterally and anteroposteriorly, and probably lengthen somewhat.

CARDIOGRAM. At the beginning of the period, the curve falls, as the auricles relax, and then rises because of the increased pressure exerted on the wall of the chest by the contracting ventricle. This rise is the best mark that we have of the instant of the beginning of the contraction.

VENOUS PULSE. The "first negative wave," seen in the early part of the period, caused by the fall of pressure in the relaxing auricle, is immediately followed by the beginning of the "second positive wave" due to the protrusion of the tricuspid valves at the beginning of the systole of the ventricle. The third heart picture, or rather one resembling it, belongs on the dotted line marking the close of this period.

CAROTID PULSE. The curve falls slightly because the blood is flowing out of the vessel into the capillaries. Occasionally a slight extra fall is seen accompanying the auricular relaxation.

THE SECOND TENTH OF A SECOND.

VALVES. The auriculoventricular valves keep closed, and are protruded into the auricles by the forceful contraction of the ventricles. The semilunar valves are opened shortly after the beginning of this period.

AURICLE. The auricle is tending to enlarge, but at the same time being encroached upon by the protrusion of the auriculoventricular valves from the contracting ventricles, and an upward push of the base of the ventricle.

VENTRICLE. The systole of the ventricles begins, and early in this period the pressure rises above that in the arteries, and the valves open, and the blood begins to pass out. The sudden tension of the muscle fibers contracting on the resisting blood causes the dull sound, which prolongs the first sound of the heart. Inasmuch as the sound does not last throughout the systole, it is unlikely that it is caused by the contraction process, as such. It is not unlikely that as the ventricle begins to contract it narrows from side to side and slightly lengthens, the base going up a little.

CARDIOGRAM. The curve is rising. The resistence of the blood in the aorta causes the hardening apex of the heart to press more firmly on the wall of the chest, and the resistance of the blood in the pulmonary artery helps to cause increased pressure on the diaphragm; (the systole causes a decided depression of the diaphragm, which is strongly felt by the hand when placed against its under surface.) Although the ventricles finally narrow in all diameters during systole, probably, at first, the narrowing is most in the lateral and anteroposterior directions, the blood being compressed by the swelling muscle, and the ventricle tends to lengthen rather than shorten.

VENOUS PULSE. The marked rise in the curve of the venous pulse, "the second positive wave," is generally attributed to the protrusion of the tricuspid valve curtains, caused by the rapidly increasing tension of the blood in the ventricle. This would hardly seem sufficient to account for the extent of the rise, although such a pressure wave, meeting the accumulating blood in the vein, would have considerable effect. It is not unlikely that in the early part of the systole the ventricle lengthens, and that

the whole floor of the auricle rising adds to the effect.

CAROTID PULSE. The primary wave begins to rise when the semilunar valve opens, that is, a short time after the beginning of this period, and 0.03-0.04 second after the beginning of the second positive wave of the venous pulse curve, the S wave, or, as it was formerly called, the C wave. This time relation, like the shape of the cardiogram and the two pulse curves, is altered by the effect of respiration. The primary wave rises rapidly and vigorously, usually to the full amount the systolic pressure can distend the artery. It is possible that the swelling of the root of the aorta, where it is in contact with the right auricle and the superior vena-cava, helps to cause the large second positive wave seen in the venous pulse curve; but as this usually starts before the primary wave of the carotid pulse, it is unlikely that the change in the arteries initiates the second positive wave.

THE THIRD TENTH OF A SECOND.

VALVES. All hold the same position.

AURICLES. The auricles are relaxing, and are being filled by the pressure of the blood accumulating in the veins. They are rapidly expanding and are being opened up by the elastic pull of lung fibers, (a pneumocardiogram shows an increase in the negative pressure in the chest due to contraction of the ventricles and this may slightly assist). Also they are filling because of the descent of the base of the ventricles, the floors of the auricles, caused by the combined effects of the shortening of the ventricles and the lengthening of the arteries, as the blood is forced into them. All this means that blood is being drawn out of the veins.

VENTRICLES. As they empty the blood into the arteries, the base of the ventricles descends at the same time that the ventricles shorten and the stretched large arteries lengthen.

CARDIOGRAM. The curve may continue to rise and may show a more or less level plateau, or may fall slightly, according to the character of the contraction of the heart and the resistance which the blood meets in the arteries.

VENOUS PULSE. The curves fall rapidly and very markedly, giving the "second negative wave." This is due to the rapid expansion of the auricles, and particularly to the rapid descent of the base of the ventricles, caused by their contraction and the lengthening of the large arteries.

CAROTID PULSE. A predicrotic wave may be seen. This is frequently an instrumental error. One thinks also of wave reflections from the periphery, and, since the aorta is in communication with the ventricle, of a wave of central origin, perhaps transmitted from the diaphram.

THE FOURTH TENTH OF A SECOND.

VALVES. Toward the end of the period, the pressure of the blood in the sinuses of valsalva, causes the curtains of the semilunar valves to approach.

AURICLES. The rapid filling during the preceding period results in a slight elastic recoil. Also they are being pressed on by the swelling roots of the arteries.

VENTRICLES. They are continuing to draw together, and are completing the filling of the arteries.

CARDIOGRAM. The curve usually falls slightly, because the ventricles as they draw together, press less strongly on the wall of the chest. (In the diagram the apex is represented as leaving the wall, which of course it never does.)

VENOUS PULSE. Frequently a slight rise of the curve occurs, the introductory part of the V wave. This has been called the first onflow wave. It may be readily confused with a wave which is an instrumental error. It may be caused by the continued accumulation of the blood in the veins, and, as seems to me more probable, to a pressure wave from the auricles, resulting from an elastic recoil following the large inflow of blood in the preceding period.

CAROTID PULSE. The systolic plateau is generally falling slightly.

THE POSTSYSTOLIC PERIOD.

VALVES. This starts with the sudden closure of the semilunar valves, caused by the rapid fall of pressure in the ventricles and the elastic recoil of the roots of the large arteries. The closure of the valves causes the second sound of the heart. The auriculoventricular valves open at the end of the period, at the instant that the pressure in the ventricles has fallen below that in the auricles. In other words this is a period during which both valves are closed.

AURICLES. These are continuing to fill from the veins. The pressure is suddenly increased by the rapid rise of the base of the relaxing ventricles.

VENTRICLES. The ventricles are rapidly relaxing, and the sudden fall of pressure results in a quick closure of the semilunar valves at the beginning of the period, and the opening of the auriculoventricular valves at the close of the period.

CARDIOGRAM. A rapid fall of the cardiogram is seen, due to the dilation of the ventricle lessening the pressure on the chest wall. The

fall is interrupted for a brief instant, and a shoulder is seen on the falling curve; this shoulder is very likely caused by a pressure wave transmitted from the roots of the large arteries, when the relaxing ventricular walls withdraw their support.

VENOUS PULSE. The "third positive," the V wave, continues to rise, and bends up quite sharply, the bend starting at a time corresponding to about the middle of the descending limb of the dicrotic notch in the carotid curve, that is, just after the beginning of the relaxation of the ventricle, and at about the time that the second sound is heard. It is caused by a pressure wave developed in the right auricle by the sudden return of the base of the ventricle. The wave is cut short by the opening of the tricuspid valves, when the pressure in the auricle suddenly falls as the blood rushes into the ventricle.

CAROTID PULSE. The fall of the curve to the dicrotic notch starts at the very beginning of the period, just after the ventricle, as shown by the beginning of the fall of the cardiogram, begins to relax. The notch is the result of the withdrawal of the support of the root of the aorta, when the ventricular wall relaxes at the beginning or diastole. The following dicrotic wave is caused by the elastic recoil of the root of the aorta.

THE FIFTH TENTH OF A SECOND.

As most of this is taken up by the post-systolic period which has been just described, it will be unnecessary to consider it further.

THE SIXTH TENTH OF A SECOND.

VALVES AND SOUNDS. The auriculoventricular valves on the right side, the tricuspids, flap together for an instant, when a large amount of blood enters the ventricle rapidly, and produce a faint sound, the third sound of the heart. The effect is supposed by Thayer to be produced by pressure waves or currents reflected back along the wall of the ventricle into the spaces behind the valve curtains. (Einthoven who, as a result of experiments with the string galvanometer, places the sound 0.13 seconds after the second sound, says that it is due to an after vibration of the semilunar valves.) Similar effects might occur in the left heart, in conditions causing an unusual accumulation of blood during systole, and following a sudden inrush at the beginning of diastole, for example by mitral insufficiency.

AURICLES. The blood is leaving the auricles and filling the ventricles.

VENTRICLES. They are enlarging rapidly and filling with the blood.

CARDIOGRAM. Shows a rise due to the pressure of the enlarging ventricles on the wall of the chest.

VENOUS PULSE. The "third negative wave," which started towards the close of the preceding period, continues its fall. It is due to the sudden lowering of the pressure in the auricle as the blood rushes into the ventricle. The fall is sometimes interrupted by a little wave, the H wave, which comes at the time that the third sound of the heart is heard, and under similar conditions. It is supposed to be due to a pressure wave caused by an elastic recoil of the wall of the ventricle, when it has been suddenly distended by the inrush of an unusually large amount of blood from the auricle.

CAROTID PULSE. Curve falling.

SEVENTH AND EIGHTH TENTH SECOND.

There is little to be said concerning these periods. Henderson has called the time from the third sound, that is, about the middle of the preceding period to the end of the cycle, the period of "diastasis." During this time the semilunar valves are closed, and the auriculoventricular valves open. It is this period that is chiefly shortened by moderate increase in heart rate. Both ventricles and auricles are at rest, and blood is flowing into them from the veins, completing the filling. The cardiogram has fallen to the base line. The venous pulse curve usually shows a slight rise due to the accumulation of blood in the veins. The carotid curve is slowly falling, as the arteries empty the rest of the blood which was received during the ventricular systole into the capillaries.

DISCUSSION.

DR. ALBION W. HEWLETT: It is very difficult to realize how much work is necessary in the preparation of such a diagram as has been shown, on account of the many divergent views that must be reviewed and reconciled. The carotid pulse which Dr. Lombard has drawn is the usual one; but when recorded by a sensitive instrument certain points of difference appear. There is a brief sharp wave preceding the main pulse wave and the dicrotic wave is also sharper and shorter than has been figured here. The study of abnormal venous pulses may throw some light on the interpretation of the normal. For example, two explanations have been given for the negative character of the normal venous pulse during ventricular systole. According to one it is due to auricular diastole, and according to the other, it is due to the descent of the base of the ventricles during ventricular systole. While both factors undoubtedly play a part in the production of the negative character of the venous pulse, there is some question as to which is the more important. During auricular fibrillation, the auricles are motionless and no diastole occurs. In such cases, the venous pulse commonly loses its negative character. It would appear from this that the diastole of the auricle is of great importance in producing the negative quality of the normal venous pulse.

DR. JAMES G. VAN ZWALUWENBURG: I should not discuss this exceedingly intricate subject if I had not spent considerable time in its study.

I am pleased to see the factor of the movements of the "base" of the heart emphasized as it deserves. It most clearly explains the phenomena of the venous pulse and of the cardiogram, and is exactly what one would expect to find from the study of the various physical factors involved, that is, the masses, velocities, inertias, etc. of the heart and its contents. Unfortunately these do not allow of mathematical expression.

I should like to extend Dr. Hewlett's comment on the carotid tracing to apply as well to the jugular. The tracing reproduced is a very typical example of a normal jugular as recorded by the ordinary instrument. However, when you use an instrument capable of recording 80 to 100 oscillations per second, the picture is quite different. It is also so variable that Dr. Agnew and I were wholly unable to reach a satisfactory solution of the problem of its analysis. It was hoped that simultaneous tracings with the intraauricular pressure curves would simplify matters. But those only introduced new problems.

One of the most important facts to be remembered in such a study is that, at the jugular, we record a volume-curve and not a pressure-curve. The distinction is a very real one. With a competent valve at the jugular bulb we may record only the results of the opening and closing during the time the valve is closed.

Altogether the problem is a very complicated one, as well as very interesting and I very much appreciate Dr. Lombard's simple exposition of the present state of our knowledge.

Dr. Lombard (closing the discussion): I would like to say that I agree thoroughly with what has been said, that the carotid curve given on the chart, although of a form frequently obtained, is not really an ideal representation of the pulse curve. The nearest approach to what seemed to me to be an ideal pulse curve, I got by dissecting out the carotid of a rabbit, tying two ligatures about it, cutting between them, and then fastening the central end to a very light bamboo lever. The artery was stretched by each beat and the elastic oscillations of the wall were well recorded. With reference to the venous pulse, I will say that I have a tracing in the laboratory which is practically a duplicate of the one given in the chart. The venous pulse varies very much and the curves are not constant. The curve shown is perhaps a fair illustration of the time and shape of the oscillations which appear in such curves.

HUMAN BLOOD SERUM THERAPY.

Howard H. Cummings, M.D.

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Chemical studies of the human blood and physiologic researches on circulation and coagulation have solved many perplexing problems, but when we consider some of the common vascular phenomena and try to explain them we realize that much remains to be done. As an example, normal coagulation of blood proves to be a complicated process. Normal blood is supposed to contain a substance called prothrombin which enters into combination with calcium salts and an enzyme of unknown chemical structure called kinase or zymoplastic substance and forms thrombin. Thrombin unites with fibrinogen forming a clot. This is a theory which appears reasonable but the clotting of blood is supposed by other workers, to be a simpler process. To explain the non-coagulation of blood in the vessels this theory goes farther and supposes that there is in the blood, a neutralizing substance to prothrombin called antithrombin. Likewise, antithrombin is supposed to be neutralized by tissue juices and thus allow clotting. In other words, the explanation of the common phenomenon, blood coagulation, is based on theory and is still unsettled. I mention this fact because in discussing the uses of human blood serum, I must admit that much is unknown regarding its action. However, is this not true in regard to some of our most useful agents? Think of the results if Jenner had failed to use the virus of cowpox because he did not understand just how it acted or its relation to smallpox. I know that there are many practitioners of medicine who know that human blood serum has been used successfully by men like Welch, but feel incompetent to use it because they have become confused in reading the literature. And this is not surprising if one is confronted by such expressions as, hemorrhage due to lack of blood platelets, antithrombin and fibrinogen; serum sickness; anaphylactic shock; deaths from serum injections; and acute hemolysis due to blood transfusion.

Human blood serum is the liquid portion of the blood after coagulation has taken place. When it is obtained from a healthy person and collected in a sterile condition it is one of our most useful therapeutic agents in combating hemorrhagic disease. I will briefly mention some of the explanations or rather theories of its action. Human blood serum when injected into a person suffering from a spontaneous hemorrhage or from persistent hemorrhage due to rupture of small vessel walls, causes cessation of bleeding. This action is supposed to be due to a shortened coagulation time or to an increased firmness of the clot. The serum injected is supposed to furnish kinase, prothrombin, calcium or fibrinogen. Whipple[1] has reported hemorrhage in a case of septicemia due to antithrombin; also a case of melena where prothrombin was absent, and a lack of fibrinogen in a fatal dose of hepatic cirrhosis. Duke[2] finds that blood clots slowly when the blood platelet count is low. Morowitz[3] believes that there is a lack of an enzyme kinase or thrombokinase. King and Stewart[4] explain slow coagulation in cases of jaundice as due to a union of calcium and bile pigment,

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1. Whipple, G. H.: Arch. Int. Med., 1912, IX, 365.
2. Duke, W. W.: The relation of blood platelets to hemorrhagic disease, Jour. Am. Med. Assn., 1910, LV, 1185.
3. Morowitz, P.: Handbuch d. Biochemischen Arbeitsmethoden E. Abderhalden, 1911, V, 223.
4. King, J. H., and Stewart, H. A.: Jour. Exper. Med., 1909, XI, 673.

free calcium being decreased. Conradi[5] has isolated a substance which inhibits coagulation; this he calls antithrombin. Summarizing all of the theories we must explain the action of blood serum in one of the following ways:

1. The introduction of blood serum supplies one or all of the substances necessary to produce coagulation.
2. Blood serum stimulates the blood forming organs to supply the substance which is lacking and causing the bleeding. This theory has been advanced by Cooley[6] in a recent paper.
3. Blood serum neutralizes anthithrombin or other toxic substances which are inhibiting coagulation.
4. Blood serum has an action on damaged cells of the vessel wall. This is believed by Welch.[7]
5. Blood serum neutralizes toxins which are damaging the vessels.

During the last three years, I have used human blood serum in a variety of cases, most of the work having been done in the department of obstetrics and gynecology of the University Hospital. A modified Welch apparatus for obtaining the serum, was used in all of the cases. I will briefly describe this simple and satisfactory devise. A small Erlenmeyer flask is fitted with a two-hole rubber stopper. Two glass tubes, one longer than the other, and both bent, are inserted into the flask. One tube which is used as a suction tube, is connected with the rubber and tip of an ordinary blood counting pipette. Inside of the rubber tube is a small glass bead which fits tightly and acts as a valve when the rubber is not forced away from it. Inside of the glass tube, a small amount of cotton is placed to prevent saliva from contaminating the interior of the flask. The second glass tube is connected by a rubber tube with a salvarsan needle. The apparatus is allowed to boil in normal salt solution for five or ten minutes, when it is ready for use.

The donor's arm is prepared and a rubber ligature passed about the arm above the elbow. The needle is thrust into the basilic vein and by making suction on the blood counter tip the flask can be filled quickly. When the required amount of blood has been obtained, the rubber cork and glass tubes are removed and the flask is plugged with sterile cotton and set away in a cool place. It is well to place the flask, slightly tilted, in a bowl lined with cotton. Within one-half hour about 20 cubic centimeters of serum will separate from 80 cubic centimeters of blood and after a few hours about one-half volume of serum will be removed. When it is necessary to act immediately, I use the fresh blood, injecting it under the skin of the abdomen, between the shoulders or into the arms or legs. In weak children a hot water bag placed over the site of injection, hastens absorption of the serum. The following facts can be relied upon in using human blood serum:

1. It is nontoxic whether given in small or large doses.
2. No anaphylactic reaction results whether injected at short or long intervals.

The histories of some of the patients treated will be of value in illustrating the use of human serum.

Case 1. Obstetric Number 675, Mrs. E. F. age 40, was admitted to the Maternity Service on April 3, 1912. The family and personal histories were negative until the present trouble which began five years before. The patient had been pregnant nine times and all had gone well until the fourth month of her eighth pregnancy, when she began to have hemorrhages from the rectum. A marked anemia developed and her physician induced labor. From that time until her present pregnancy she had been free from the rectal hemorrhages but they had returned during the fifth and sixth months of this pregnancy. An examination showed a very anemic woman about seven months pregnant. There was edema of the whole body and marked pigmentation of the skin. A rectal examination showed dilated vessels in a very pale mucosa and in some places blood could be seen in the mucosa, but no actual ulceration was visible. The hemoglobin reading by the Miescher apparatus was 23 per cent. with a corresponding low blood count. Examination of the stools gave a strong blood test. The first nine days the patient was given a daily injection of 20 cubic centimeters of blood serum. At the end of this time no blood could be found in the stools. The injections were discontinued and blood soon reappeared in the stools. At the end of three weeks the patient's hemoglobin was 28 per cent. The daily dose of blood serum was increased to 30 or 40 cubic centimeters and the patient improved. On May 22, she went into labor prematurely, the hemoglobin being at this time 40 per cent. This patient received over 600 cubic centimeters of human blood serum and nearly every man in the senior class donated blood. Premature rupture of the membranes occurred with prolapse of an arm and the cord. The patient did not report the accident until the child was dead and a shoulder had become impacted. She was delivered manually without anesthesia and made a good convalescence.

The interesting feature of this case was the prompt disappearance of blood in the stools when serum was used, and its reappearance when the injections were discontinued.

5. Conradi, H.: Beitr. z. Chem. Phys. l. c. Path., 1902, 136.
6. Cooley, T. B.: The treatment of hemorrhagic disorders. Jour. Am. Med. Assn., LXI, 1277.
7. Welch, J. F.: Am. Jour. Med. Sc. 1910, CXXXIX, 180.

CASE 2. Gynecologic Number 4832. Mrs. M. M., age 47, had borne two children and had been well until nine years before entrance when her menstruation became profuse and three years later she noticed a firm, smooth tumor arising in the median line of the abdomen. The flowing had increased until it had become almost constant. The patient showed generalized edema, and a marked secondary anemia with a hemoglobin reading between 10-12 per cent. Miescher. She had a hydropic fibroid of the uterus and ascites. The patient was flowing when admitted on February 20, 1913 and the next day 30 cubic centimeters of human blood serum was injected. On the third day the flowing had ceased and the patient was given injections of blood serum at intervals of a few days. She also received the usual treatment of rest in bed, Blaud's pills, sunlight and wholesome diet. In slightly over three weeks, the hemoglobin estimation was 42 per cent. and the patient was operated upon and cured. In the ward at the same time were two patients with fibroids and severe anemia due to bleeding. These patients were also kept in bed, in the sunshine when possible, given Blaud's pills and a wholesome diet. They improved but not so rapidly as the patient treated with the serum.

CASE 3. Gynecologic Number 4728. Miss F. P. age 13 years, entered the hospital January 2, 1913, suffering from menorrhagia which began about six months before. The periods appeared about every two weeks and she would flow from eight to fourteen days. A curettage was performed but the endometrium proved to be negative. In May, 1913, she returned because the profuse flowing had reappeared. She was treated for twenty days with daily injections of 10 cubic centimeters of human blood serum and thirty grains of calcium lactate. The flowing ceased and did not recur during her stay in the hospital. The subsequent history is not known.

CASE 4. Gynecologic Number 5144. A young girl age 18, giving the same history as the one just related, was treated with human blood serum, horse serum, and calcium lactate. The bleeding was controlled but the patient spent several uncomfortable days with her giant urticarial wheals.

Human blood serum in cases of melena has come to hold the position of a specific remedy since Welch's[8] splendid report, given in 1910. The results are nearly all uniformly good and the surprising feature is the control of bleeding by relatively small doses. I have treated but one case of melena; the result of the serum therapy was good.

In 1912, Welch[9] called attention to the value of human blood serum in cases of malnutrition in infants. The following case will illustrate its value:

CASE 5. Obstetric Number 661. Miss S., age 18, gave birth to a premature infant at the eighth month. The child's birth weight was about 4½ pounds or 2025 grams. The child nursed well until the twelfth day when it was nearly back to normal weight. Then he began to refuse nourishment and lost in weight very rapidly until at the thirty-second day, he weighed 1600 grams, having lost 404 grams in eighteen days. It was evident that the child was doomed if he continued his downward course for a few more days, so daily injections of 8 cubic centimeters of human blood serum were given. The first day the child gained 46 grams and each day he gained from 25 to 50 grams and was back to his birth weight after ten days of treatment. In the next sixteen days he gained 600 grams and was discharged when fifty-eight days old. Two other premature children were treated with blood serum and responded well.

I wish to relate the history of another patient.

CASE 6. I was called by Dr. John Holmes to administer blood serum to E. P., a boy, 9 years of age, who was having whooping cough and for three days had had a continuous epistaxis. This lad also had a congenital heart lesion which had been diagnosed as a persistent ductus arteriosus. A history of hemophilia in the males of the mother's family was obtained. An examination revealed a very anemic boy with a rapid heart rate. The nose was filled with soft clots and gauze packing. Perchloride of iron had been used in the nose, but there was a continuous slow ooze of blood from the nostrils.

The father gave some blood and 10 cubic centimeters of blood serum were injected into the boy's abdominal wall. A second injection was given one hour later. Within two hours the bleeding had practically ceased. Five days later the bleeding began again, but was promptly checked by giving 15 cubic centimeters of serum. The boy made a splendid recovery.

It is neither scientific nor right to draw conclusions from single cases but surely the histories reported suggest that human blood serum has a place in modern treatment. I do not wish to convey the idea that I consider human blood serum a panacea, for in three patients suffering from carcinoma of the cervix and bleeding profusely, I could not see a beneficial action. A child with a cerebral hemorrhage was treated but later died from pneumonia. I have tried human blood serum in a case of acute enteritis in a child of two years, but other treatments given at the same time made it impossible to note the effect.

8. Welch, J. E.: Am. Jour. Med. Sc. 1910, CXXXIX, 800.
9. Welch J. E.: Am. Jour. Obst. 1912, LXV, 597.

The injection of human blood serum does not compete with direct transfusion. The indications for direct transfusion of blood are clear. When a larger amount of blood is lost within a short time, or where red corpuscles are needed to carry nourishment to the vital centers, transfusion and not serum injection is indicated. Billings[10] believes that when a hemorrhage has not endangered a person's life, human blood serum rather than direct transfusion should be used. Vaughan[11] mentions the fact that transfusions are rather frequently done when the simple administration of serum would answer equally as well.

In hemophilia and melena neonatorum human blood serum has proven its great value, but I believe that this field of therapy is broader than we know and that many lives will be saved by it.

Malnutrition in infants has always been a stubborn condition and when far advanced, has frequently proven fatal. Here, human blood serum should be tried. In the cases observed it has operated as if by magic.

The injection of human serum in women with myomata and suffering from anemia severe enough to offer an obstacle to operative work is a large field. If the bleeding is controlled for a few weeks the blood condition will so improve as to make the operation without great risk. Esch[12] has reported three cases where he used defibrinated blood to control the hemorrhage from myomata. With three injections of 15, 20 and 22 cubic centimeters, he was able to raise the hemoglobin from 25 to 46 per cent. The three patients survived their operations. Esch[13] used defibrinated blood in treating a case of pernicious anemia occurring in the puerperium.

Surgeons have always dreaded operations upon jaundiced patients because of the frequency of primary and secondary hemorrhage. Not all jaundiced patients bleed but the liability is greatly increased. Undoubtedly here is a useful place for human blood serum therapy. Meyer[14] and others have reported excellent results where the serum was given for several days preceding the operation and in doses of from 30 to 60 cubic centimeters.

It is questionable whether human blood serum or the transfusion of blood can greatly benefit patients with pernicious anemia. The frequency of megaloblastic showers and the associated improvement make one suspect that the cures reported were only the better phase of this disease. However, in secondary anemias, whether the source of the loss of blood is apparent or hidden, human blood serum offers great possibilities.

In closing let me say that with a therapeutic agent so abundant and so harmless and with a method so simple no physician should hesitate to try human blood serum. Serum from healthy individuals is absolutely safe to inject.

DISCUSSION.

Dr. Reuben Peterson: This work of Dr. Cummings is not only interesting but of great importance. Serum therapy is especially indicated in the two classes of cases mentioned, bleeding fibroids, and melena neonatorum. If the uterine hemorrhage can be stopped great good can be accomplished with large doses of iron, but it is not always easy to control the bleeding by packing, for the hemorrhage may be high up in the uterine canal. In patients with hemoglobin below twenty per cent. it is dangerous to curette under an anesthetic. In such cases human blood serum should always be tried and usually will be found efficacious. Just before the publication of Welch's paper, I had a case in private practice which undoubtedly could have been saved by serum therapy. It is magical to see how cases of bleeding in the new born respond to injections of blood serum and fortunately they can be administered without danger.

Dr. R. Bishop Canfield: I have had considerable experience with the use of horse serum, but have used human serum in but one case and that in the hopes of building up the patient's resistance to infection. There is a new preparation of calcium known as calcine, which has seemed to be of decided importance in reducing the coagulation period. This substance injected directly into the buttock eight hours before an operation in which one expects to encounter hemorrhage seems to be of decided value.

Dr. John T. Holmes: The patient I had Dr. Cummings see was a case of whooping cough in a child who had epistaxis and was in a very critical condition. I decided to start in with serum injections. We gave him fifteen cubic centimeters of serum with very good results, for the next day the hemorrhage had stopped. The child remained in fairly good condition for four or five days and then the hemorrhage started again. We gave another injection of serum and the child finally got well and is now in fairly good health. This condition was associated with a heart lesion which the child had had since birth. Dr. Marshall saw the case later and thought it was probably a patent ductus arteriosus.

Dr. Warren P. Lombard: I would like to ask Dr. Cummings what he regards as the cause of the increase in hemoglobin. I wonder whether by taking the blood from healthy individuals you got just what was needed. I wish to ask if the blood of the patient had been analyzed, and whether in any of the cases where the blood had been examined a lack of calcium had been found. I wonder whether the giving of calcium would have done the business.

Dr. Cummings (closing the discussion): I believe there is a field for human blood serum in cases of malnutrition. Welch has reported several cases where the serum was used successfully and our results were entirely satisfactory.

In answer to Dr. Lombard's questions, I would say that the cause of the rapid increase in hemoglobin is the cessation of the hemorrhage. It has been suggested that the serum stimulates the blood forming organs.

10. Billings, F.: Internal Hemorrhages: Can we control them? Jour. Am. Med. Assn., 1913, LXI.

11. Vaughan J. W.: Direct blood transfusion, Jour. Mich. State Med. Soc. XII, 582.

12. Esch. P.: München. med. Wchnschr., 1911, LVIII, 2154.

13. Esch P.: Deutsch med. Wchnschr. Berlin XXXVII.

14. Meyer, Wiley: Surg., Gynec. and Obst., 1911, XIII, 152.

THE NEW CONTAGIOUS HOSPITAL AT THE UNIVERSITY OF MICHIGAN AND ITS PROPOSED PLAN OF OPERATION.

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Within a few weeks the new contagious pavilion of our Hospital will be fully equipped and ready to receive patients. It seems fitting, therefore, that a brief description of the building and its proposed plan of operation be submitted to the members of this Society, since we one and all are interested in seeing it a success.

It will be remembered that a year ago last August it was voted that the city of Ann Arbor bond itself for the sum of twenty-five thousand dollars for a contagious hospital. This sum of money was given outright to the University with the understanding that in return the latter was to furnish the land for the building, purchase the equipment and maintain the hospital. The city was to be charged the usual hospital rates for room, board and nursing of contagious patients, while medical attendance was to be free.

For many years both the city and the University have been in great need of a contagious hospital. The former has found it a very expensive proposition to care for its contagious patients, since it was obliged to pay the maximum price for medical attendance and nursing in this class of patients. House quarantines have been difficult to maintain and on the whole unsatisfactory, with the result that the city in the past has suffered from not a few contagious disease epidemics.

The University has been in even a worse condition as regards contagious disease. House quarantining of students not only was ineffective but meant great loss to the students and the University. The University Hospital at times has suffered a great deal from different contagious epidemics which on a number of occasions has led to the quarantining for months of certain portions of the Hospital. These quarantines not only meant a great pecuniary loss to the Hospital but greatly interfered with the clinical teaching.

Again, the University was anxious for a contagious hospital in order that it might be utilized for demonstrating contagious diseases to the senior medical students. Owing to the remarkable development and growth of the University Hospital during the past ten years, the members of the clinical faculty have had at their disposal a wealth of material for teaching purposes except in thi sone particular. Again and again has the faculty pointed out to the University authorities the need of the proper facilities for the teaching of contagious disease, so that the University was ready for the hospital and willing to meet the city half way in order that both might be benefitted.

Fig. 1. University of Michigan Contagious Hospital.

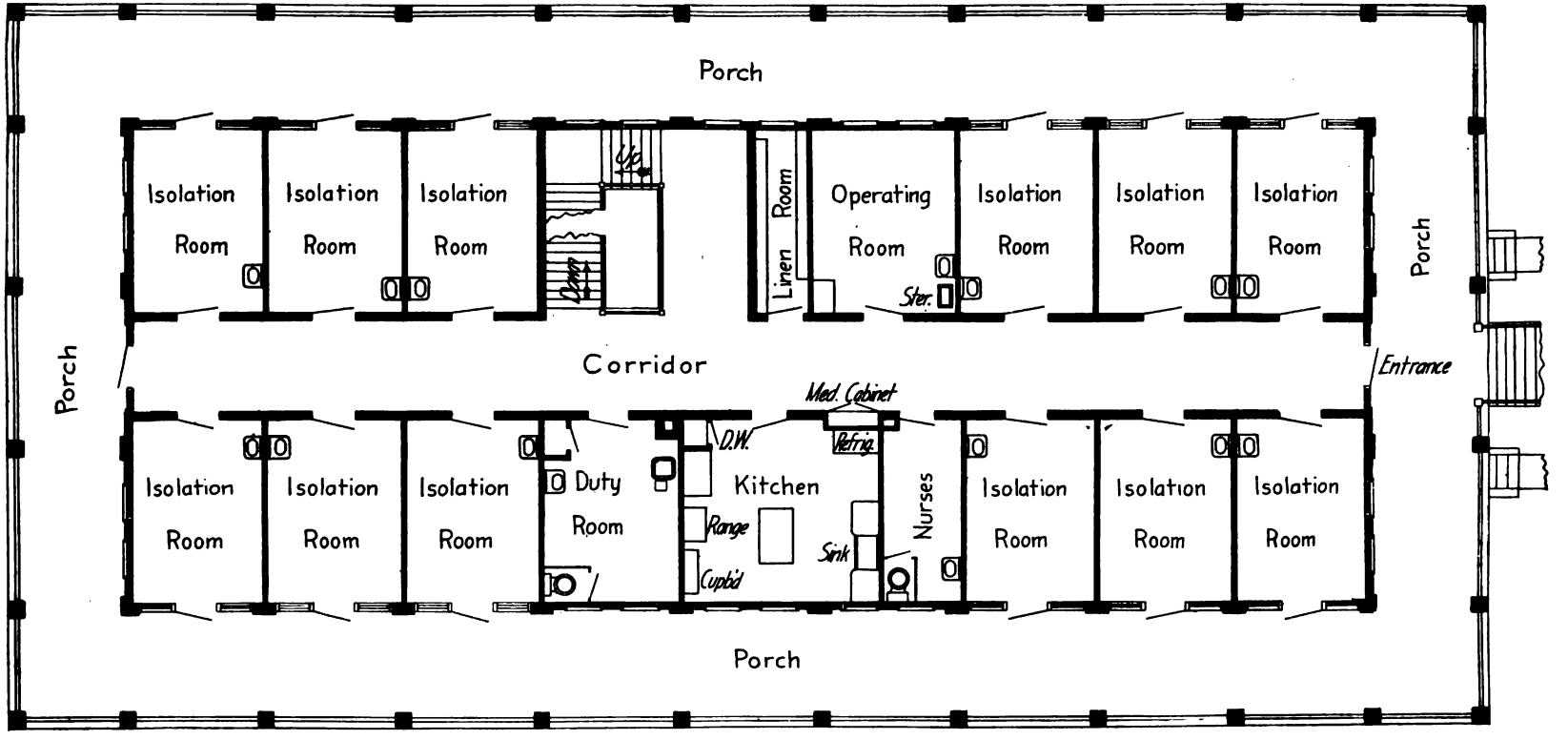
In order to meet the needs of both city and University the following had to be provided for:

1. The building or buildings must be so constructed as to accommodate patients with all varieties of contagious diseases.

2. The hospital must be so planned as to allow of the utilization of the patients for teaching purposes.

I distinctly remember the first plans submitted without solicitation to Dr. Hewlett and myself. These plans provided for three separate hospital units for patients with three separate contagious diseases. Each unit had its own administration and utility rooms and each opened by a separate corridor into a spacious amphi-

Fig. 2.



FIRST FLOOR

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theater, where the patient was to be demonstrated to a class of students seated behind a glass partition. In these early days of the consideration of our problem this plan seemed a gem. There was only one hitch. The estimated cost of the hospital was from seventy-five to one hundred thousand dollars, three or four times the sum at our disposal. After discussing a scheme of asking the Regents for fifty thousand dollars to supplement the twenty-five thousand gift from the city and for obvious reasons giving up this plan as impracticable, it was decided to let the matter rest until after your medical director's visit to the east where he was to look into the contagious disease question, as applied to our problem.

I will not weary you with a detailed description of my trip and the many contagious hospitals I visited, but will endeavor to give you the results of this study. I found that the experts in the hospital care of contagious diseases were pretty well agreed that infection was not air-borne but was transmitted from one person to another by actual contact. By this is meant the virus producing the contagious disease is in reality deposited upon or within the person, who through this means contracts the contagious disease. From this it follows that if such conveyance from one person to another could be prevented by the proper technic, cross infection would not take place in a contagious hospital, even if patients with different contagious diseases were in the same building or even in the same room.

Fig. 3. View of porch on west side of building looking south.

Nearly all of the experts referred to the pioneer work of Grancher who showed that infection is not air-borne but is from contact. They cited the examples of the French and English hospitals in the care of contagious diseases. In the Pasteur hospital in Paris the patients are kept in small cubicles in the same room and although the same nurses care for patients

suffering from different contagious disease, cross infection has been reduced to a minimum by taking precautions to sterilize everything which has come in contact with the patient.

While, as I have said, nearly all the experts were in accord that infection arose chiefly from contact, most of them did not have the courage of their convictions. In the same hospital you would see the patients cared for in accordance with the theory that infection was conveyed by contact but also that it was air-borne as well. Unconsciously they were unable to rid themselves of the old ideas regarding infection, as shown by elaborate arrangements by means of adjustable partitions for preventing the air of one room from mingling with that of another.

Now this hesitancy to accept *in toto* or at least to put in practice the principles of the theory that infection is carried by contact was very familiar to me because of my experience in surgery. My hospital experience dates back to the time when the disinfection of the air of the operating room was still practiced. As an intern it was part of my duties to see that the carbolic vaporizer was thoroughly used the day preceding the operation. This was soon given up but it required many years of actual experience before surgeons became convinced once and for all that the air of the operating room had nothing whatever to do with surgical infection. The latter results from actual contact so that if the surgeon be sure that everything coming in contact with the wound is sterile, he is practically certain no wound infection will result.

Thus the theory of infection by contact as regards the contagious diseases appealed to me in two ways: First, it was in accord with my surgical experience and looked reasonable; second, if cross infection of contagious diseases could be reduced to a minimum by a system of medical asepsis, our problem here at the University Hospital was practically solved, since it meant that all kinds of contagious diseases could be treated in the same building. For one thing was certain: For the sum at our disposal, twenty-five thousand dollars, it was out of the question to erect a separate building for each contagious disease with all the duplication of administration rooms such separate buildings would entail.

Finally, in the course of my investigations I

Fig. 4. Photograph of an isolation room looking toward the central corridor.

reached the Providence City Hospital where I was overjoyed to find in actual operation, in accordance with the principles of the infection by contact theory, a pavilion which, with some changes, could be utilized for our purposes. The Providence City Hospital is a municipal hospital for the care of contagious diseases. The buildings have been designed under the supervision of Dr. Charles C. Chapin, Superintendent of Health of Providence. Doctor Chapin has been a health officer for thirty years and is an exceedingly competent man. He is a firm believer in the theory of infection by contact, as may be seen by a perusal of his valuable book, "The Source and Modes of Infection." A recent article of his in the February 7th number of the *Journal of the American Medical Association* entitled, "The Air as a Vehicle of Infection" is of especial interest in connection with our subject.

Dr. L. R. Richardson, the superintendent of the hospital, is also a very able man and is courtesy itself when it comes to placing at the disposal of medical visitors the results of medical asepsis in the treatment of contagious diseases. Not only did he spend a great deal of [illegible] with me explaining the system under which the pavilion referred to is conducted but he has been of the greatest practical help to us in the drawing up of the plans of our contagious hospital.

The pavilion referred to is known as the Isolation Building, in which are placed doubtful or mixed cases of scarlet fever, diphtheria, chicken pox, whooping cough, rubella, mumps, measles and miscellaneous cases of infectious disease. The technic of this building is based upon the principles of aseptic nursing. The infection is confined to the rooms occupied by the patients, while the utility rooms and the central corridors are considered to be as free from contagion as are those of any general hospital. The same nurses, observing aseptic precautions, care for all patients. The interesting fact in connection with this building is that the technic employed has been proved to be eminently satisfactory, since only a very small percentage of cross infection has occurred among the large number of patients treated in this building. Since it is proposed to adopt practically the same technic in our own hospital as that in use at the Providence City Hospital, the details will be omitted until our hospital plan has been discussed.

Fig. 5. Photograph of an isolation room looking toward the porch.

As you are aware, our contagious pavilion is situated to the east and slightly north of the Psychopathic Hospital. This site was selected by the Board of Regents for the following reasons:

1. It was the best site available in that it provided for a maximum amount of fresh air and sunlight, both of which are highly desirable in the treatment of contagious diseases.

2. It was near enough to the general hospital and its power plant to provide for tunnel connections at a minimum cost. At the outset it was realized that separate kitchen, heating and lighting plants for the new hospital would be very expensive, so far as maintenance is concerned. As soon as possible it is proposed to connect the building with the main hospital by a tunnel not only large enough to convey steam and electric light mains, but also to allow of traffic. In this way it will be perfectly possible to convey food to the pavilion from the main kitchen, besides providing a protected passage-way from the main hospital for nurses, doctors, students and employees. Such a tunnel is absolutely necessary if the pavilion is to be utilized to the greatest advantage.

The building itself has been designed by Mr. J. H. Marks, Superintendent of the university buildings and grounds department in accordance with the suggestions submitted by the members of the medical faculty and your medical director. (Fig. 1). The provisional plans were sent to six or eight well known experts in contagious diseases with a request for suggestions and criticisms. In fact every effort has been made to make the building in every way practical and useful. Undoubtedly mistakes have been made, for no hospital is ever perfect, but at least those designing the building have known what they wanted and have considered each point in detail.

From the outset it was felt that the hospital should accommodate at least twenty-four patients. This capacity has been kept constantly in mind and when it was seen that the cost of the building was going to exceed twenty-five thousand, a cut was made in the construction, rather than in the number of hospital beds. Many things have been omitted which would have gone in had a larger sum of money been available. But the orders of the Board of Regents were not to expend a dollar beyond the sum received from the city. During the planning and construction of the hospital this seemed rather a hard ruling but after all perhaps it is just as well for as a result it shows how much can be done in hospital construction for twenty-five thousand dollars.

The hospital runs north and south, is of the bungalow type and is of semi-fire proof construction. It is 103 feet long and 40 feet wide exclusive of a ten foot porch surrounding the entire building and on a level with the first floor. All bearings are of brick or concrete and all bearing members other than these are of steel. The roof construction is not fire proof which, considering the many points of egress from the building, does not seem necessary from a personal hazard standpoint. The heating plant is designed for steam to be furnished eventually from the central plant through a tunnel which will also serve as a passage-way to the building from the general hospital. The electric lighting is of the old direct type though the wiring is adequate for the indirect system in case this be decided later to be desirable. No expense has been spared on the plumbing, the materials and fixtures of which are the best obtainable. The concrete and plumbing work was done by contract, the electric wiring and painting being done by the University. From the standpoint of construction the building is very satisfactory, all workmanship being first class.

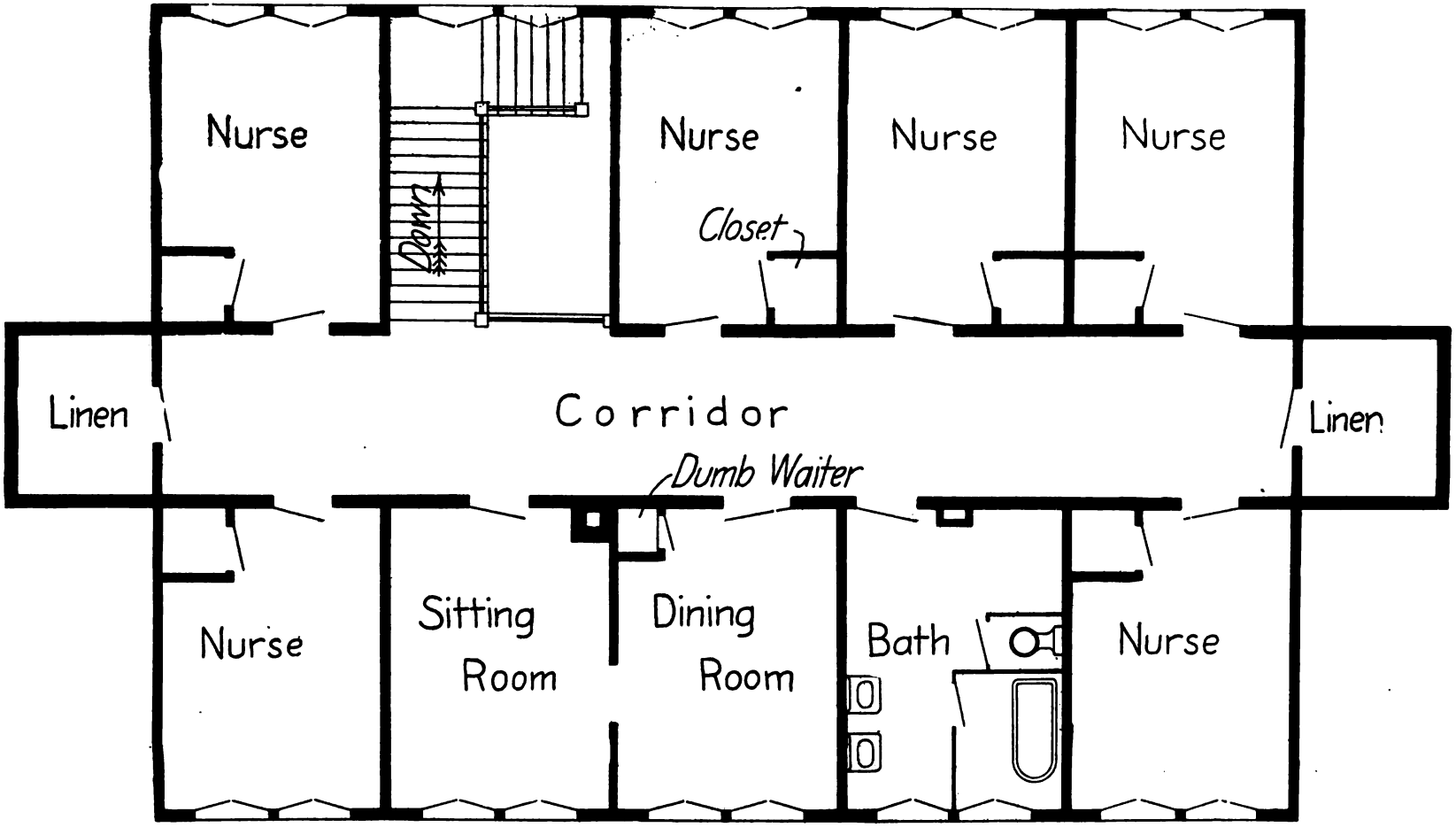
The first floor (Fig. 2) is entirely given over to patients and service rooms. The latter, consisting of utility, bath and operating rooms are situated in the center and are therefore readily accessible to the patients' rooms which are located at either end of the building. These twelve rooms are of the same size, 12 by 16 feet, and each can easily accommodate two persons.

Each room opens upon the ten foot porch by means of a door wide enough for the passage of an ordinary hospital bed. (Figs. 3 and 5). On each side of this door are windows over which are situated transoms. The upper half of the door, opening upon the central corridor, is also of glass. The result is an abundance of light for each room in spite of the covered porch.

Each room is furnished with a lavatory where the hot and cold water is regulated by a knee pressure device. The furniture of the rooms is to be of the simplest. It will consist of two iron beds, two bed side stands, two enameled chairs, shelf for towels, soap retainer worked by foot pedal, brackets for wash basins holding solution, two small shelves for toilet articles, and wall hooks for nurses' gowns. (Figs. 4 and 5).

In order to avoid a common error of hospital construction, the utility room and diet kitchen have been made especially large. The operating room is also of good size. The linen closet, situated in the center of the building next to the hallway is plenty large enough for the supplies of twenty-four patients. The bath room was intentionally made small since the common use of such a room was impossible with men and women patients on one floor. Even with two bath rooms patients with different contagious diseases could hardly use the same toilets without great danger of infection. When bedside bathing is necessary it will be done by means

Fig. 6.



SECOND FLOOR

of a portable bath tub which will be emptied and sterilized after each use.

In the summer the entire porch will be screened. This will permit of the free opening of the doors and windows leading to the porch and insure plenty of fresh air.

The second floor has been arranged to accommodate twelve nurses. (Fig. 6). Besides the six bedrooms, each of sufficient size for two nurses, there is a dining room, a comfortable sitting room and adequate toilet facilities.

The entire basement with the exception of the morgue and laboratory has been given over to sterilization purposes. (Fig. 7). On the east side of the central corridor will be installed a most complete hospital fumigating and sterilization plant. Here will be disinfected the mattresses and the laundry before it is taken to the main hospital laundry. In the same apparatus articles impossible of sterilization by high pressure steam can be disinfected by formaldehyde vapor. Leading from this sterilizing plant will be a storage room for disinfected mattresses. The rooms across the hall have been arranged into infected and uncontaminated rooms for doctors, nurses, students and employees. The clean rooms will be plentifully supplied with steel lockers in which can be placed the street clothing of those entering the hospital. All these rooms have abundant lavatory facilities, so that all infectious material can be removed before the workers don their street clothing.

On the same side with these rooms is a patients' dismissal room equipped with a bath tub and lavatory, where the patient is thoroughly sterilized before entering the patients' locker room in which his disinfected clothing has been placed.

The floor of the porch has been made high enough and the grading so arranged as to allow of four-foot windows in the basement. These windows together with the white painted walls furnish light in abundance.

The main hospital entrance is at the south end of the building. This entrance leads to the basement and the first floor. There is no elevator in the building, the different floors being connected by a wide central stairway. A large dumb-waiter runs from the tunnel entrance in the basement, through the diet kitchen on the first floor to the nurses' dining room on the second floor.

The success or failure of the hospital under its proposed plan of operation will depend largely upon how the nursing staff carries out the principles of medical asepsis. The nurses will be in charge of one of our own graduates, an excellent executive who has spent months in perfecting herself in the technic which has proved so satisfactory at the Providence City Hospital. Before the hospital is opened the nursing staff will be thoroughly drilled in the principles of medical asepsis. Just as in the surgical operating room they will be taught that the conveyance of any infectious material to those free from disease may and probably will result in infection. They will be told that if they contract a contagious disease while on the contagious diseases service, it will be through their own or their associates' fault. Just as it is impossible for a well trained nurse to brush back her hair in the operating room or touch articles not surgically clean, so it will become impossible for the nurse drilled in medical asepsis, who has cared for a contagious patient, to touch anything until her hands have been thoroughly sterilized.

The nurse on entering the room to care for her patient will put on a gown, in order to avoid accidental contamination of her clothing. After attending to her patient she will remove her gown and thoroughly sterilize her hands and arms in running water and liquid soap, obtained from a retainer worked by a foot pedal so that the infected hands do not need to touch the receptacle. After immersing the hands and arms in some mild but effective antiseptic solution, the nurse can leave the room confident that she will not carry contagion to another patient. The main corridor is free from infection and is kept so.

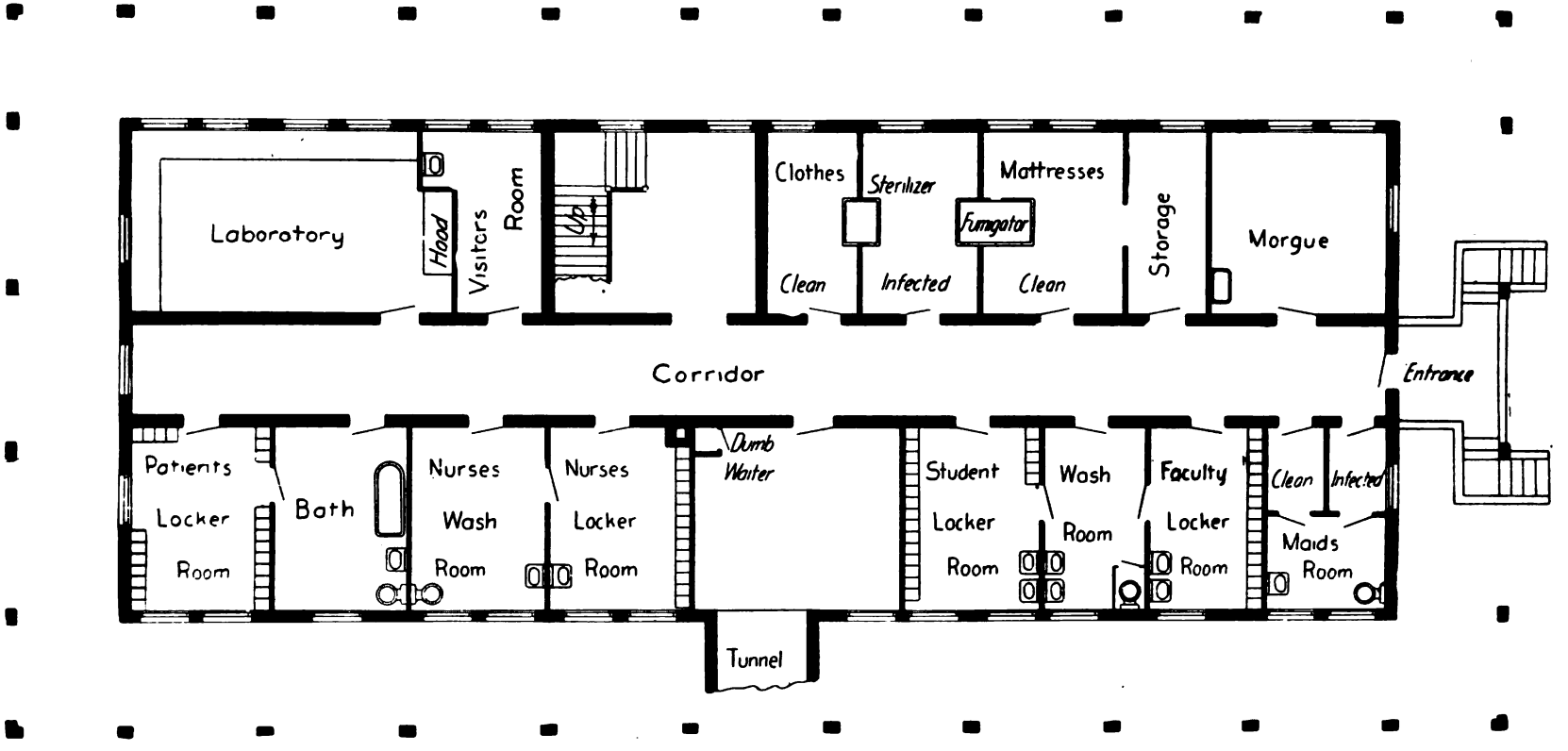
All dishes and other utensils used in the patients' rooms are immediately sterilized by steam or strong carbolic solutions. Patients' night clothing and bedding are placed in canvas receptacles and carried to the fumigating plant where they are sterilized, receptacles and all.

Extra precautions will be required of the nurses before they leave the building or retire to their rooms. In order to avoid a great danger of infection they will be prohibited from eating while on the wards. They will be served in their own dining room on dishes which have been boiled and with food that has not come in contact with any contagion. Because of a possibility of a slip in the technic and the acquiring of a contagious disease, illness of any kind among the nurses on duty will be carefully observed and if necessary the nurse will be isolated for observation.

The contagious service will not be made compulsory for any pupil nurse but, if history repeats itself, when the pupil nurse feels that if she carefully carries out a certain technic, there is very slight danger of contracting a contagious disease, she will be loath to forego such valuable experience.

One of the most valuable features of the hospital is the porch which can be made serviceable in many ways. Since each room opens upon the porch by a door through which a bed can be wheeled each patient is assured at all times of abundant open air treatment. Such a porch does away with the necessity of a pa-

Fig. 7.



BASEMENT

tients' receiving and examining room, since each patient can be admitted directly to his room by way of this porch. Care will have to be exercised to keep porch patients with different contagious diseases from infecting each other. However, this can be prevented by means of movable screens which can serve as barriers.

It is felt that from a teaching standpoint the building will be particularly serviceable. It is proposed to demonstrate the contagious diseases patients to the students in sections. It certainly seems ridiculous to demonstrate such diseases to students behind glass partitions for fear of infection during June of the senior year and then expect such students to care for patients with similar diseases July 1st, after the students have graduated and entered upon their practice. Just as the student, drilled in surgical asepsis, is taught how to wash his hands and refrain from touching anything surgically unclean during an operation, he will be thoroughly drilled in the principles of medical asepsis, so that he neither will convey infection from one patient to another nor contract it himself.

The student will be gowned when he enters the patient's room for fear of accidental contamination. Otherwise, unless he handles or touches the patient, a gown would be unnecessary. After the patient has been visited the gown is removed and the hands and arms carefully washed. The street clothing is then resumed and the student can leave the building without fear of carrying contagion with him.

Fig. 8. Photograph of central corridor, first floor. Although the patients' rooms open upon this central corridor, the latter will be as free from infection as those in a general hospital.

The porch will be found especially serviceable when a single patient or a series of patients must be shown to the whole class in too short a time to allow of section demonstration. By means of the porch and the glass doors and windows of each room such patients can easily be demonstrated to a class of a hundred or more students in a very short time.

When a room is emptied it will not be dis-

infected by fumigation. No part of the Isolation Building at Providence has ever been fumigated and the good results speak for themselves. If there be nothing to the theory that infection is air-borne, then the air of the room in which the contagious patient has been is as free from organisms as is that of any other room. To make the room free from the possibility of infecting another patient who may occupy it, the bedding, the mattresses, the bed, the walls as far as the patient can reach, in fact, everything which the patient could have touched must be disinfected. It has been shown that this can be very thoroughly done by scrubbing with soap and water. The room should be well aired before it is occupied, just as we would thoroughly air a room recently occupied by a patient with a non-contagious disease.

Let me say in conclusion that there will be cross infection under any system of the hospital care of contagious patients. There is cross infection when a separate hospital unit is employed for each contagious disease. Undoubtedly there will be some cross infection under the plan proposed, but it will be very slight provided those having to do with the hospital are careful as regards the technic. It is in your hands to demonstrate how in a teaching hospital a contagious pavilion with all kinds of contagious patients can be conducted with a minimum amount of cross infection.

DISCUSSION.

DR. HOWARD H. CUMMINGS: The new contagious hospital will be of great value to the senior medical students and will aid greatly in the work of the University Health Service. As many of you know, the Regents have provided a way whereby students, ill and needing hospital care, can be sent to the hospital and remain for sixty days if necessary. During this year we have had cases of measles, mumps, chicken-pox, whooping cough, diphtheria, Vincent's angina, tuberculosis and pneumonia. In the last two weeks, we have treated forty cases of epidemic sore throat. All of these patients could have been cared for in this hospital.

DR. JOHN A. WESSINGER (Health Officer): The matter will be governed by first come, first served. There may be a time when there are twenty-four patients in the hospital, all students, and when there is no room for city patients. We can't help that. First come, first-served. And there may be a time when the hospital is full of city patients and there is no room for students. In my opinion it will be some time before all rooms in the contagious hospital are filled at one time, and when that time comes, it will be time enough to make preparations for another building, or rather an addition to the present building.

DR. PETERSON (closing the discussion): The University authorities will soon submit to the city the scale of charges for patients treated in the contagious hospital. It goes without saying that these charges will be made as reasonable as possible, since the University is not trying to make money out of any portion of its Hospital. It must be remembered that on account of extra laundry and other things needed in the care of contagious patients the cost of maintenance of this class of patients is higher than with the ordinary hospital patients. I am sure all patients, whether they be university students, city charges, or citizens of Ann Arbor, will be treated alike and that the administrative policy of this new pavilion will be satisfactory to all concerned.

SOME POINTS OF INTEREST IN INGUINAL AND FEMORAL HERNIA.

CYRENUS G. DARLING, M.D.

Clinical Professor of Surgery, University of Michigan. (From the Surgical Clinic, University Hospital, Ann Arbor, Michigan.)

There are many theories concerning the formation of hernias and nearly all, more or less, contain a bit of truth. Andrews believes that a well developed abdomen rarely fails in its function of retaining its contents perfectly and it is strange that the strains put upon the abdominal wall should not more frequently cause a giving way of the wall. He believes that congenital defects and injuries are the cause of nearly all abdominal hernias.

Dr. Ochsner in a recent article on hernia in children holds to the theory of inside pressure and advances many good reasons in support of his belief. He admits, however, that a faulty development of the abdominal wall and an unclosed tunica vaginalis may be to some extent the result of inheritance. On the other hand Bernstein says the theory that intraabdominal pressure causes the hernia is probably overthrown today. Roser thinks that the sac is primary and the contents secondary.

Bernstein calls attention to the presence of depressions in the peritoneum, which he calls hernial anlage as being of great importance in the formation of hernias. He found that in a large number of bodies examined that 25.8 per cent. had a hernia or hernial anlage.

Linhard advances the theory that femoral hernia is frequently caused by lipomata advancing through the ring and pulling the peritoneum with it to form the sac.

Many other theories might be mentioned, but with the above in mind, during the last few months I have examined patients during the operation for the following:

First, for the presence of hernial anlage in the inguinal or femoral regions.

Second, the presence of lipomata preceding or associated with the hernial sac.

Third, any abnormal or unusual conditions associated with operations for the cure of hernia.

In median line operations when one has the hand in the abdomen depressions in the peritoneum can be easily detected at the site of the femoral or the inguinal openings or in both at the same time. I always make a point of examining the right side when operating for chronic appendicitis and in one instance this

habit was of value. This was in the case of a young man with a vague history of sudden and short attacks of appendicitis. I readily found the inguinal depression and passed my index finger into the canal. The tissues seemed to grasp my finger and suggested what might happen to an inclosed piece of bowel. Was not this patient suffering from repeated attacks of hernia instead of appendicitis? I removed both sac and appendix and did not experiment for an answer.

The results of these examinations coincide with those of Bernstein as about one in four contained one depression and in one case, four were found.

A young man twenty-one years old, a night watchman, while running, fell forward striking his right inguinal canal against a hard substance. There was some soreness, but not enough to interfere with lifting heavy bags the next day and the day following. Two days after the fall he noticed a swelling in the right side, not painful, but unusual. He went to see his physician about it and he diagnosed a hernia. It was irreducible and remained this way for about three weeks when one morning he found that it had suddenly disappeared. He reported this fact to his physician, who advised him to go at once to the University Hospital for operation.

At the Hospital he was asked as usual to produce his hernia, but to no effect. Curiosity and the desire to do the man some good, led me to operate in the absence of a hernial tumor. Nothing unusual was found until the inguinal canal was opened. Near the lower end of the canal in close relation with the cord was what appeared to be a hernial sac. When this was opened about thirty drops of clear fluid escaped. This was a cyst without an opening, but there was a prolongation of tissue, such as composed its wall, back through the internal ring. When this prolongation of tissue was opened, a small canal was found through which a grooved director could be passed into the abdominal cavity. The bruising of the lower end of this canal formed a cyst, which under sufficient pressure, could empty along the canal into the abdomen and showed conclusively that a very narrow sac from the peritoneal cavity was present, only requiring sufficient force from above to convert it into a hernia.

Another of a similar type was in a man of forty-five years old, with what appeared to be a right femoral hernia, which could be reduced by firm continuous pressure. After the skin incision, the fat was carefully separated from the sac so that it was entirely exposed. The sac was then opened and about two drams of clear fluid removed. Examination of the interior of the sac disclosed a small opening through which a grooved director could be passed into the peritoneal cavity. This opening had a valve action, which allowed the fluid to flow freely from the abdominal cavity to the sac, but did not permit it to return.

It would seem that in some instances hydrocele of the cord might be formed in the same manner, especially in cases of congenital hernia, or even in cases that appeared some time after birth where the hernia had been reduced and a truss worn for some time. This case also presented the mass of subperitoneal fat, which is supposed to be carried down in front of the peritoneum.

Another case was that of a student, twenty-three years old, operated under local anesthesia for right femoral hernia. There was a large amount of fat in the space below the femoral ring in which the sac was buried. As the opening was very large, some of the fat, together with the stump of the sac, was inverted to plug the opening. The tissues were separated from the femoral vein for the purpose of exposing it so that it might not be injured by the suture and also for the purpose of securing a firm fascia, which when sutured to that on the opposite side of the opening would effectually and firmly hold the tissues in the canal.

In some of these cases of femoral hernia, the mass of fat was large enough to be called a tumor. In two cases it seemed like an independent tumor but careful dissection revealed within the remains of a sac. It would seem that in some instances the small elongated sac had never contained anything but fluid. Yet they must be considered as possibilities for the development of hernia if proper pressure is exerted from within.

I recently saw a case of strangulated femoral hernia in Professor de Nancrède's clinic, which presented some interesting points. The patient was a syphilitic, and very anemic with 35 per cent. hemoglobin. The hernia had been strangulated but a short time and no attempt had been made at reduction: The fat which surrounded the sac was quite edematous and the lymphatic nodes around the femoral opening showed the usual enlargement found in the secondary stage of syphilis. The edema was probably caused by the interrupted circulation and the anemia. There was no discoloration of the tissues.

In another case operated at the University Hospital, I followed the advice of Dressman, opening the sac close to the internal ring. On the posterior and outer side of the sac was a depression or diverticulum back of the neck of the sac, such as is found inside of the abdomen. It was about one-half inch deep. Though the hernia had no particular relation to this depression, it may have started in another depression lower down.

Can hernia be cured by wearing a well adjusted truss? I operated upon a case where a truss had been worn for some time. When the inguinal canal was opened, the patient vomited, but nothing came down into the sac. This gave a fine exhibition of the way the transversalis and internal oblique muscles can hold the abdominal contents back when they are both impaired and the ring not expanded. This seemed like a so-called cure through wearing a truss, but the sac was readily found on the inner side of the cord. When opened, a very narrow neck was found not large enough to let the intestine through in its present condition. The other side was reported to have shown a hernia at one time and there was some difficulty experienced in producing a sac. When it was found there were two small cysts at the lower end definitely separated from the sac either of which might have increased in size if injured. A truss had never been worn on this side and the patient had no knowledge of the injury. I cannot explain the origin of these cysts.

A young Italian laborer, very muscular, was thrown forward. In the attempt to save himself from falling an inguinal hernia was produced. The hernia was immediately reduced and a truss applied but he was unable to wear it. He was operated for the hernia on the sixth day after the accident. The external oblique fascia was unusually firm and strong. The conjoined tendon was a real tendon and all the tissues seemed perfect. The sac extended down into the scrotum and was exceedingly thin. There was a well defined neck to this sac, which was red, infiltrated with some plastic exudate on the peritoneal side. There was no difficulty in reducing the hernia when the truss was applied. Was this a preformed sac, which was injured when the hernia was formed or was the change in the tissues due to injury from the truss which was in position but a few hours?

There is nothing new in my recorded observations of these cases, but like many instances in research, they may help to confirm or destroy the theory of some other investigator. The evidence is strong in favor of the preformed sac, in part at least, in most cases of inguinal and femoral hernia.

Linhard's theory, that muscular action first moulds a piece of fat through the femoral ring, which in turn pulls down the peritoneum thus forming a sac, may not be entirely true, but in a large number of cases the fat is there and in some instances the amount is large enough to be called a tumor.

A truss never cures hernia and except for temporary use should be abolished.

My most important point can be mentioned only for discussion. If hernia is a congenital deformity or is acquired through no fault of the owner then the State should extend to him the privilege of an operation without expense, provided he is not able to pay for same.

DISCUSSION.

DR. REUBEN PETERSON: As a contribution to the subject discussed by Dr. Darling, I wish to cite my findings in several hundred cases of shortening the round ligaments after opening the inguinal canals. I cannot give my statistics off hand, but in quite a few cases hernial sacs were found where the opening into the peritoneal cavity was so small as to preclude the passage of any bowel through the internal ring. In a number of instances the sacs were cystic and the condition undoubtedly congenital.

DR. R. A. MCGARRY: In regard to the cause of hernia I would like to suggest that as a predisposing factor, embryonic development may play some part in it. An over development, or excessive amount of peritoneum, should be considered. In cadavers we often find conditions suggesting this, as an exceptionally long common mesentery, or long mesocolon.

REPORT OF CASE OF DERMOID CYST OF THE ORBIT, PRODUCING MARKED EXOPHTHALMOS, RELIEVED BY THE KRONLEIN OPERATION.

WALTER R. PARKER, M.D.

Professor of Ophthalmology, University of Michigan.
(From the Ophthalmic Clinic, University Hospital, Ann Arbor, Michigan.)

History.—The patient, Mrs. S., aged 30, came to the clinic January 21, 1914, complaining of prominence of the left eye. The family and personal history were negative. The left eye was noticed to be larger than the right about twenty years ago, but there was not much change until six years ago, when the exophthalmos rapidly became more marked till in a few months it assumed the present condition. About five years ago there was some pain in the eye and a progressive failure of vision began.

Examination.—Vision right eye, 5/4, left eye faint light perception. The pupillary reflexes were present. Tension, right eye, 20 millimeters Hg., left eye, 4 millimeters Hg. The right eye showed no external pathology. The left eye showed marked proptosis, measurement with the exophthalmometer reading, right eye 12, left eye 35. The anterior pole of the cornea was one-half inch below the level of a corresponding point of the right eye, and was nearly on the level with the bridge of the nose. The eyeball while not enlarged was nearly all anterior to the boundaries of the orbit which was filled with a somewhat slightly movable mass. Indefinite pulsation was detected above and there was indistinct fluctuation temporarily. The insertion of the external rectus was fairly well marked and its action could be plainly seen. The movements of the eye were limited in all directions, especially in abduction.

The lids were enlarged but freely movable. The upper lid at rest completely covered the cornea leaving an elongated aperture of about one quarter inch between the upper and lower lid borders.

The palpebral and ocular conjunctiva were only slightly congested. The fornix was occupied by loose vascular tissue showing distinct venous engorgement, and above were large venous plexuses. The cornea, iris and anterior chamber were practically normal.

Ophthalmoscopic Examination.—The right eye showed a few vitreous opacites but was otherwise normal. The left eye showed a distinct secondary optic atrophy, with a pale avascular nerve head. The retinal vessels showed some tortuosity. There was a large area showing choroidal changes situated above the disc and a peculiar striated arrangements of pigment extending down and around the macula.

Blood and urinary examinations were negative.

X-Ray Report.—Maxillary and frontal sinuses open, unusually large size. On the left side, the orbit is filled with a relatively dense mass, causing a distinct depression of the lower floor and apparent elevation of the roof. Sphenoid cell is not involved. Some opacity in the neighborhood of the ethmoids. Sella turcica normal.

Wassermann test reported positive by one test, negative by another.

Otolaryngologic Report.—Very large middle turbinate on left side. There were no signs of tumor in the nose. Transillumination shows nothing on account of tumor.

Diagnosis.—The slow growth of the tumor, absence of fluctuation, compressibility, and pulsation, together with the normal sinuses as shown by the otolaryngologic and X-Ray reports lead to the diagnosis of benign tumor situated entirely within the orbit—the exact nature of which not determined. (Fig. 1).

Fig. I. Case of Dermoid Cyst of the Orbit before Operation.

Operation.—A wide skin incision about three inches long, semicircular in shape, convexity forward, was made temporarily. A Krönlein resection of the outer wall of the orbit was done, a portion of the malar bone removed. The periosteum was dissected free from the outer orbital wall at its margin. The tumor mass was accidentally ruptured with the escape of a large amount of brown serous fluid causing a marked recession of the eyeball. By blunt dissection the whole of the cyst sac was easily freed from the periorbital and the muscle cone, except near the apex where it was more firmly adherent to the periosteum. The deeper contents of the sac consisted of a brownish liquid, and thin pultaceous material containing fragments

of hair. There was practically no orbital fat, and after the cyst was removed an unobstructed view could be had to the apex of the orbit. The wound was closed with silkworm and horsehair sutures without drainage. The eyelids were united by a single suture.

Postoperative History.—The postoperative recovery was uneventful except for some edema of the lids and conjunctiva which was controlled by pressure bandage. The proptosis was reduced from the first. When the stitches were removed about one-half dram of straw colored fluid escaped from the incision near the outer canthus but no infection nor reaccumulation of fluid resulted.

an exceedingly rare occurrence. The commonest position is near the upper and outer angle of the orbit overlying the frontomalar or the frontotemporal suture. They are frequently found at the upper and inner angle of the orbit overlying the frontoethmoidal suture. When found lying at some depth in the orbit, they are external to the muscle cone, and closely connected with the muscles, the eyeball, the sheath of the optic nerve, or the periosteum. Although situated deep in the orbit they may have their origin at the orbital margin. Their contents are well known to consist of epithelial debris, sebaceous material and hairs. In rare cases a tooth has been found.

Fig. 2. Case of Demoid Cyst of the Orbit after Operation.

The last examination shows ptosis from lack of cushion and eyeball markedly convergent and displaced down about 11 millimeters. The eyeball can be rotated just beyond the medium line. The eyeball is normal in appearance. (Fig. 2).

Pathologic Report.—Old dermoid into which there has been a hemorrhage. Destruction of the epidermis, with but a few dead hairs remaining in the wall. Much cholesterin.

Dermoid cysts are always congenital. They are regarded as fetal structures resulting from the invagination or involution of the external blastodermic membrane. They are by no means rare in the conjunctiva or at the orbital margin, but to find one in the orbit leading to an exophthalmos as in the case here reported is

As a rule, on account of their superficial situation, they do not displace the eyeball, but push forward the skin of the lid through which they can be readily felt as round movable tumors. When they are situated deep in the orbit the diagnosis becomes more difficult; especially is this the case if the cyst wall has become so tense as to make the pressure or absence of fluctuation indefinite. The history of the case will at once eliminate the possibility of a malignant tumor. Meningocele and encephalocele are two congenital conditions which must be eliminated as possibilities before operating. The first is a prolapse or hernia of the meninges with cerebrospinal fluid contents, projecting through a breech in the retaining skull wall. The second is the same with the addition of

brain substance prolapsing within the meningeal sac. Both are reducible and after reduction the bony margins of the aperture through which they came can be felt. Pulsation and hemic sounds can be elicited. The size and tension is variable. A dermoid cyst will present none of these phenomena. If the cystic nature of the tumor can be established, without pulsation, a mucocele having its origin in one of the accessory sinuses must be considered as a possibility.

When the cysts are superficial, they can usually be extirpated without difficulty. But when the process extends deep into the orbit complete removal may be difficult. If the whole cyst is in the orbit, as was the condition in the case here reported, the best mode of procedure is a Krönlein's temporary resection of the external orbital wall.

TRANSACTIONS
OF THE
CLINICAL SOCIETY
OF THE
UNIVERSITY OF MICHIGAN

STATED MEETING, APRIL 15, 1914

THE PRESIDENT, R. BISHOP CANFIELD, M.D., IN THE CHAIR
REPORTED BY REUBEN PETERSON, M.D., SECRETARY

Reading of Papers

(1) A CASE OF NON-GRAVID HYDRORRHEA DUE TO HYSTERIA.
(2) A CASE OF ABDOMINAL CESAREAN SECTION FOR CONTRACTED PELVIS IN A CHILD OF TWELVE.
(3) A CASE OF ABDOMINAL CESAREAN SECTION AT THE SEVENTH MONTH FOR THREATENED ECLAMPSIA.

REUBEN PETERSON, M.D.
(From the Obstetric and Gynecologic Clinic, University Hospital, Ann Arbor, Michigan).

CASE 1. A CASE OF NON-GRAVID HYDRORRHEA DUE TO HYSTERIA.

Mrs. E. W., gynecologic number 5260, married, age 25, referred by Dr. C. Peabody, Lake Odessa, Michigan, entered the Obstetric and Gynecologic Clinic of the University Hospital September 29, 1913.

History.—The family history is negative. Her health was excellent up to the time of her marriage at the age of 19. She says she had meningitis three years ago and was very sick for six weeks but made a good recovery. She gives no history of luetic or Neisser infection. Menstruation was established at the age of fourteen and has always been regular and painless.

She has one child six years old. Her pregnancy was uneventful except for slight hemorrhage and the leaking of the waters at the sixth month. However, she carried the child to full term and was delivered by instruments after a labor extending over two days. She was quite badly lacerated, but was not repaired. She was in bed three weeks and was not well for three months. About a year ago she aborted at the fifth week from some unknown cause. She was curetted and made a good recovery.

She comes to the Hospital for headache, pain in the lower abdomen and across the back. These symptoms have been present since her child birth six years ago and have been much worse since she had a second attack of measles in the spring of 1913.

The pain in the abdomen is dull in character and worse when she is lying down. For the past few months she has suffered from a leucorrheal discharge, which at times requires the wearing of a napkin but has never had a foul odor nor has been blood streaked.

Since July, 1913, the abdomen has seemed to swell just before the period. This enlargement subsides after she has flowed two days. This is followed by a discharge from the vagina of a large amount, at times as much as two quarts, of watery, slightly bloody fluid. Ten days ago shreds of tissue or membrane came away after the flow. With the last few periods she has had some nausea and vomiting. She does not consider herself very nervous. Since last spring she has lost ten pounds in weight.

Examination.—An examination made the day of entrance showed the abdomen to be negative except for tenderness in the left lower quadrant. Percussion gave tympany throughout. The perineum was lacerated and there was a cystocele and rectocele on straining. The uterus was completely retroverted and there was a bilateral laceration of the cervix. The appendages could not be outlined on account of tenderness.

On October 3, 1913, the uterus was dilated and curetted and the cervix and perineum repaired. The abdomen was then opened and the appendages found normal. The uterus was held forward by a modified Simpson shortening of the round ligaments.

The pathologic examination showed marked glandular hyperplasia of the cervix with decidedly cystic glands with a glandular erosion. The endometrium showed glandular hyperplasia of the non-resolution type.

The patient made a good recovery, her abdominal wound healing by primary union.

There was at times considerable abdominal distension which was thought to be due to gas. She was discharged from the Hospital October 21, 1913.

It is of interest to note that her physician in the letter accompanying the patient to the Hospital speaks of the accumulation and discharge by the vagina of large amounts of serum which he thought came from a tubal infection dating back to the time of her abortion. While the fluid was accumulating there was severe abdominal, cramping pain which ceased after the discharge of the fluid by way of the vagina.

Six days after leaving the Hospital the patient wrote that she was suffering from considerable abdominal pain and distension.

November 1, she wrote that the distension suddenly went down leaving her with much pain across the lower abdomen. The pain lasted three or four days and was relieved by the discharge of about a pint of clear fluid from the vagina. She remarks that this is what she had before the operation and asks if something cannot be done for her relief.

Up to this time the case had not seemed out of the ordinary since it was not uncommon for women before and after abdominal operations to complain of distension and transitory pains. The history of profuse vaginal discharges also is not uncommon. Investigation usually reveals the cause of the discharge or shows that its importance, amount and character have been overestimated by the patient.

However, there was a distinctly different element in this case. The patient undoubtedly passed considerable quantities of watery fluid from the vagina or bladder, the discharge being preceded by abdominal distension and cramping pains. A sample of this fluid was sent to the Hospital by her physician and examined in the medical laboratory. It was slightly turbid with a high specific gravity and contained a considerable amount of albumin and nucleo-albumin. It contained neither mucin, paramucin, sugar nor blood. The microscopic examination was negative owing to contamination by boric acid placed in the fluid for preservative purposes. The report closes with the following:

"We have no suggestion to offer as to what this fluid might be. It certainly is not from a cyst and we are certain it is not urine because it contains only three grams of urea per liter and this could easily come from the albumin present in the fluid."

A second specimen was examined in the medical laboratory December 21, 1913, with the following report:

"We wish to report the fluid that came from Mrs. W. It is a greyish opalescent fluid with a flocculent greyish white sediment. Specific gravity of the fluid is 1002, acid reaction, it requiring 4 cubic centimeters of tenth normal NaOH to neutralize 100 cubic centimeters of fluid. It coagulates upon boiling and does not reduce Fehling's solution, does not precipitate with acetic acid in cold (mucin). Urea .91 grams per liter. The examination of the sediment shows that it is composed almost entirely of bacteria of which by far the greater number are bacilli. There are present a few acid fast bacilli, which, however, decolorize with alcohol, making it likely that they are smegma bacilli.

Dr. Hewlett is of the opinion that this is not urine.

The following letter from the patient dated December 7, 1913, is interesting: "You asked me to write if that fluid gathered in my abdomen again. It began to gather last Tuesday and part of the fluid came away Friday afternoon. There was about three ounces, half of which Dr. Peabody sent you. I began having pain Friday morning and by afternoon it was so severe I called the doctor. He gave me two 'hypos' before I felt any relief, but as soon as the effect of them wore away the pain was as bad as ever, until Saturday a pint more of the fluid came. Then I felt relieved and could sleep. Before the first fluid came I was filled so high I could hardly breathe. This is the second time it has gathered between periods. It seems to require so much more hard pain before it will discharge than at the periods. There seems to be some swelling in the left side of the abdomen over the left hip bone and across the back. Trusting you may find the cause of the trouble, I remain etc."

Surely a well written and intelligent letter from a woman with a condition which is giving rise at irregular intervals to considerable suffering.

During December the patient grew worse, the attacks becoming more frequent and the pain more severe. The physicians in attendance thought they could detect bulging in the posterior culdesac. As the patient was becoming more and more prostrated by the attacks and seemed to be failing fast, it was deemed best to send her back to the Hospital which she reentered December 26, 1913.

The patient was examined soon after entrance, at which time she was having some abdominal pain. The night before there had been severe pain in the left side and leg. The patient's abdomen was greatly distended and tympanitic throughout. Toward night the pain had become very severe. There were paroxysmal attacks of abdominal pain closely resembling the pains of labor. The patient emptied the bladder every twenty minutes to one half hour. The urine was clear, contained a large amount of epithelium and a considerable number of white cells. The specific gravity was 1003. During the attack she became nauseated and vomited a small amount of mucus. The pain became so severe

as to prevent the patient from lying down. She would walk back and forth, occasionally bending over with the pain. In six hours' time she passed thirty-eight ounces of urine. Between seven and eight in the evening she felt something give way inside of her and a moderate amount of fluid came away from below. The patient was immediately relieved and the abdominal distension subsided. At nine o'clock a second small amount of fluid came away and one half hour later the patient was very comfortable, although she had some pain in the left side and leg. Examination on day of entrance was practically negative with the exception of some abdominal tenderness and sensitiveness in the region of the appendages. The latter were not enlarged nor adherent.

From December 26, 1913, to January 16, 1914, the date of the second operation, the patient had frequent attacks similar to those described above. Always the attacks would begin with abdominal distension and paroxysmal pains. Then would come the feeling as of something breaking or giving away. This would be followed by a discharge of fluid from below, whether from the vagina or urethra the patient was unable to say. Then would follow subsidence of the abdominal distension and relief of the paroxysmal pains.

December 30, 1913, at the beginning of one of these attacks in order to determine definitely whether the fluid came from the vagina or urethra, the vagina was packed with dry colorless gauze and a solution of methylene blue injected into the bladder. When the "break" came the night dress was found to be wet with a clear fluid and urine immediately afterward was colored with the methylene blue. The gauze removed from the vagina was without color, though soaked by a clear fluid. This fluid was sufficient in amount to wet the glove, but not enough for examination.

During another attack the cervix was examined through a speculum and fluid was seen coming from the external os.

In order to eliminate still further the urinary tract as the cause of her attacks the patient was referred to the Genito-Urinary and X-Ray departments. A skiagraph taken after catheterization of the ureters and injection of the urinary tract with collargol showed the pelvis of the kidneys and the ureters perfectly normal.

January 16, the uterus was again dilated and curetted, very little tissue coming away. Although bimanual examination showed no abnormality of the appendages it was deemed best to explore the pelvis a second time. This was done through an anterior colpotomy incision. Thorough palpation of both tubes and ovaries showed them to be perfectly normal.

The pathologist reported that aside from slight interstitial changes of recent regeneration the endometrium was practically negative and that there was nothing to explain the origin of the fluid.

When the patient came out of the anesthetic she was told that the cause of her trouble had been discovered and that she would not have any further discharges of fluid. From the date of the operation to her discharge from the Hospital twelve days later there were no further attacks.

I have heard from the patient and her physician within the past week. The patient has been absolutely free from the attacks of hydrorrhea since her discharge from the Hospital three months ago.

It seems to me as if we were justified in making a diagnosis of hydrorrhea of hysterical origin by the method of exclusion.

It was proved by examination that the fluid came from the cervix and not from the urinary tract. The pelvis, as shown by two explorations, was free from cysts or fluid collections in or about the tubes. The history of the case subsequent to the second operation also bears out the diagnosis, since through suggestion the attacks ceased.

Hydrorrhea is occasionally observed in the pregnant woman and is due to the hyperplasia of the glandular structures of the decidua. There is a profuse secretion of clear fluid which is continuously discharged or may be retained within the uterus and suddenly discharged in large quantities. Hydrorrhea in the non-puerperal woman is certainly a rare and obscure condition. The microscopic picture of the endometrium in the present case while showing glandular hyperplasia seemed to throw very little light on the source of the fluid which undoubtedly came from the uterus.

In the Surgeon General's Catalogue there are five references to the condition, to three of which I have had access in the university library.

J. Oliver in the *British Medical Journal,* 1884, says that patients suffering from non-gravid hydrorrhea are usually of a nervous temperament. The quantity of the fluid varies, as much as six ounces being discharged at one gush with repetition at intervals of four to six hours. The circumstances attending the watery discharge are variable. In some cases there is pain in the hypogastric region frequently followed by a bearing down pain. The discharge may come from the Fallopian tubes, although more likely to arise from the uterus. The changes in this organ may be compared with those occurring in the kidneys during the secretion of the so-called hysterical urine. The condition is most probably dependent upon some derangement of innervation either of the vasomotor system or directly through the nerves which preside over secretion. Oliver is inclined to the latter hypothesis.

H. J. Garrigues reports a case of non-gravid hydrorrhea in the *Medical Record,* 1886 The patient was twenty-nine years old and the mother of two children. She was exceedingly nervous and suffered from nausea. The first attack of hydrorrhea in March, 1883, lasted three days. The second began in April and lasted six months and then ceased for three months. Subsequently it appeared only after menstruation which occurred every three weeks and lasted three days. For two months the patient did not menstruate but in its place was a watery discharge which lasted three days, the patient soaking as many as forty napkins a day. During the attacks the uterus was enlarged and tender. The tubes were not enlarged and there was no pelvic tumor. The elements found in the fluid were purely uterine in character. The condition was evidently due to endometritis and the patient was cured by treating this condition.

W. J. Mackie also reports a case of non-gravid hydrorrhea in the *British Medical Journal.* 1884. The attack followed an abortion associated with persistent hemorrhage for which ergot was administered. The hemorrhage ceased and was succeeded by the discharge of a colorless fluid. Later there were occasional gushes of clear fluid associated with nervous phenomena. There were also attacks of severe gastralgia followed by collapse. The pain was relieved by an escape of fluid from the vagina when the patient was placed in a hot bath. There were symptoms of angina pectoris accompanied by general abdominal distension. These symptoms were most frequently relieved by a gush of fluid from the vagina. The exciting causes of her attacks were over-exertion, cold, mental worry, sudden shock, anger, fatigue, et cetera. The attacks continued for some years becoming less frequent as she became stronger. There was no enlargement of the uterus at the time of the abdominal distension and the hydrorrhea was never accompanied by expulsive pains. There was an apparent vicarious relationship between the hydrorrhea and the secretion of hysterical urine. After the patient's health improved the abdominal enlargement subsided gradually. The author thinks the chief etiologic factor in the case was the marked neurotic condition of the patient.

In the present case we have a patient who becomes subject to attacks of abdominal distension and cramping pains relieved by the escape of considerable quantities of fluid from the vagina. The attacks ceased after the uterus was dilated and curetted. However, they began again after her return home before the endometrium had had a chance to regenerate. The attacks ceased again after the second curettage and determination by exploration a second time that the pelvis was normal.

The abdominal pains undoubtedly were real and were due to the accumulation of fluid within the uterus, since they were relieved by the discharge of fluid by the vagina. The cessation of the attacks through suggestion would lead one to think that the attacks probably were due to a neurosis. This seems more probable when we consider that thousands of women have been shown to have similar microscopic changes in the endometrium yet have not had similar attacks.

CASE 2. A CASE OF ABDOMINAL CESAREAN SECTION FOR GENERALLY CONTRACTED PELVIS IN A CHILD OF TWELVE.

I report this case since it is rather unusual for abdominal Cesarean section to be performed upon so young a patient. She had menstruated but once and this just before conception occurred.

The patient was undeveloped and small for her age, her weight being 91 pounds and her height 4 feet 9 inches. The pelvic measurements were all below normal, the external conjugate being 15.5 centimeters and the conjugate vera between 8 and 9 centimeters.

As far as could be judged the child was of average size and the question naturally arose whether to give the child mother a test of labor or to perform an elective Cesarean section. The latter operation was decided upon on account of the extreme youth of the mother who would be saved the possible shock resulting from a protracted labor. From the standpoint of the child Cesarean section was the operation of choice.

The operation was performed March 31, 1914, ether being administered after the abdomen was prepared. At the request of my assistant, Dr. Seeley, who has been studying the action of pituitrin in the Maternity ward a hypodermatic injection of this drug was administered to the patient about three minutes before the abdominal wall was incised. The uterus was markedly contracted even before it was opened and the child extracted. The latter was cyanotic when removed from the uterus and quite asphyxiated. It was finally resuscitated after ten or fifteen minutes of artificial respiration. So firmly was the uterus contracted that the posterior wall and placental site were turned outward through the uterine incision during the liberation and removal of the placenta. There was less bleeding than usual from the uterine wall.

The child was a healthy male, weighing about six pounds at birth. The patient had an uninterrupted convalescence and was discharged from the Maternity April 21, 1914.

I can not but feel that the wisest course was pursued with this patient. Of course it is possible that she might have had a fairly easy labor and given birth to her six pound child without

temporary or permanent injury to either. But this is looking backwards not forwards. Only approximately can the size of the fetus in utero be determined and while a child weighing six pounds is below the average birth weight, it was a large child for this particular pelvis and I doubt if it could have been delivered alive. Even had this been possible the chances of injury to the child mother would have been considerable. Far better was it for this much abused patient with her undeveloped pelvis to be spared the uncertainties and agonies of labor by submitting to abdominal Cesarean section.

From my experience with pituitrin in this case I would never use it again in connection with Cesarean section prior to the removal of the placenta.

I can see why so many unfavorable reports have been made as to the action of pituitrin. Prior to the completion of the first stage, through its powerful action on the uterus the fetal circulation is interfered with and the fetus may perish in utero before the beginning of the second stage. After the dilatation of the os the same may be true if the drug be administered except just before the birth of the child.

Since Dr. Seeley proposes to lay before the Society the results of his experience with pituitrin, I will not now discuss the subject further except to emphasize what has been shown by the case reported, that the administration of pituitrin may be very dangerous to the child.

CASE 3. A CASE OF ABDOMINAL CESAREAN SECTION AT THE SEVENTH MONTH FOR THREATENED ECLAMPSIA.

Although the indications for abdominal Cesarean section upon good scientific reasons are being extended rapidly, the operation is not often resorted to for threatened eclampsia. For that reason each case should be reported and the indication for the operation fully set forth.

February 4, 1914, I was called by Dr. Cowie to see in consultation Mrs. W., aged twenty-eight, advanced six months in her first pregnancy. During the early months of gestation her urine had been examined regularly and as late as December 30 had been found perfectly normal. January 31, a small amount of albumin was present but no casts. Inquiry brought out the fact that the patient for several days previous had had a food intoxication. At the time of this examination there was some edema of the ankles and upper eyelids. Examination of the urine February 3, showed 5.7 grams of albumin to the liter with numerous hyalin and granular casts in spite of the fact that the patient's diet had been restricted.

Examination at the time of the consultation showed a woman of good build with only slight indications of the intoxication of pregnancy. The patient had no headache, nor dimness of vision. Her color was good and there was only slight edema of the ankles. The uterus was at the level of the umbilicus and apparently the gestation was normal. The patient laughed at the idea of her being sick and complained bitterly of her restricted diet. At the time of this examination it was learned that the patient had been severely ill with scarlet fever at the age of fourteen. Both she and her mother thought that the kidneys had not been affected by the disease.

Although the patient was kept in bed and on a milk diet, the bowels kept open and the proper diuretics administered, the condition of the patient as shown by her urine and edema steadily grew worse. The amount of albumin increased until the precipitate was solid by the heat and nitric acid tests. The casts increased in variety and number. The patient became markedly edematous and there were evidences of quite a large amount of ascites. The blood pressure rose during the month from 150 to 180.

Since the patient's condition was steadily growing worse in spite of all treatment, evacuation of the uterus had to be considered, if eclampsia was to be avoided. While the patient naturally was very desirous of saving her child, the family insisted that her life had been placed in sufficient jeopardy and that the pregnancy be terminated in such a manner as to give her the best chances.

It seemed to me that even at the seventh month the fetus must be considered in deciding upon the nature of the operation to be performed. While the chances were in favor of the mother's condition acting unfavorably upon the fetus to such an extent as to make it problematic whether such a seven months fetus would survive, there was no way of definitely determining the strength or vitality of the fetus. That it was alive and not in extremis was shown by the regularity and strength of the fetal heart beat. Hence it seemed only fair to choose an operation which, while not lessening the mother's chances, would inflict the minimum trauma and shock upon the fetus.

Abdominal Cesarean section met both indications. It could be quickly performed, necessitating a short anesthesia which would be good for both mother and child. There was no other operation so advantageous as far as the child was concerned and no other more advantageous for the mother.

The operation was performed at my private hospital March 4, 1914. In order to save time everything was made ready for the abdominal incision before the anesthetic was administered. The abdominal incision was made below the umbilicus on account of the small size of the uterus. The abdominal wall was very edematous and there was a large amount of ascitic fluid in the abdominal cavity. This was evacuat-

ed, the uterus incised and the child extracted. It was small and puny but reacted after emersion in hot water. Every effort was made to save its life but to no purpose since death occured suddenly on the third day.

The mother had an uninterrupted convalescence. The urine gradually cleared up until it was free from albumin and casts and the patient was discharged from the hospital three weeks after the operation.

A question of some importance has been put to me by this patient. Would a second pregnancy mean a recurrence of the trouble which caused the loss of the baby and seriously menaced her own life? I have replied that in all probability it will depend upon the cause of the intoxication. If it were due to the kidney of pregnancy, it does not mean necessarily that she will be threatened with eclampsia in a second pregnancy. If, on the other hand, the renal condition was due to the attack of scarlet fever in all probability the kidneys will be affected by a subsequent pregnancy. Possibly delicate tests of the urine may settle the diagnosis since the kidney of pregnancy completely recovers while this is not necessarily true of the kidney damaged by the scarlet fever poison.

DISCUSSION.

DR. WARD F. SEELEY: In the first case the literature is so very incomplete that there is not much to add. In the second case the extreme youth of the patient is one of the interesting features. Haller reports a patient who menstruated regularly from the age of three years and was delivered of a full term child at the age of nine years. The administration of pituitrin in Cesarean section before the delivery of the child in our opinion is distinctly contraindicated. Its administration, even in normal cases, is frequently associated with asphyxia neonatorum which is probably due to marked constriction of the placental site with a consequent hypercarbonization of the fetal blood.

TWO CASES OF PARAPLEGIA OPERATION FOLLOWED BY IMPROVEMENT.

CARL D. CAMP, M.D.

(From the Clinic of Nervous Diseases, University Hospital, Ann Arbor, Michigan).

CASE 1. A woman, age 57 years, was first admitted to the University Hospital, May 5, 1913, complaining of pain of a neuralgic character in the left arm and some disability in the use of the left arm and hand. The family and previous medical history of the patient contained nothing of importance. The pain began about five months before her admission to the Hospital. Examination at that time showed a marked atrophy of the small muscles of the left hand and some atrophy of the forearm. The patient could only partially flex the fingers but other movements could be performed, though they were weak, especially flexion at the elbow. There was no weakness nor atrophy in the right arm or in the legs. Tendon reflexes in the upper and lower extremities were normal and there were no sensory changes. The plantar reflexes were normal. The right pupil was larger than the left but both reacted promptly to light and in accommodation. The left pupil did not dilate to sensory stimulation of the neck and under homatropine the right pupil dilated much more feebly than the left. The fundi showed beginning arteriosclerotic changes. The physical examination was negative and there was no deformity of the spine. Examination of the blood and urine was negative. The blood pressure was 160 millimeters Hg. and the Wassermann reaction on the blood was negative. An X-Ray examination of the cervical region showed nothing abnormal. There was no cervical rib.

The condition at first suggested was the lower arm type of brachial plexus palsy but there was no apparent etiology for this, no history of injury, no cervical rib and the pupillary signs which indicated the involvement of the sympathetic fibers showed that the lesion must involve the nerve roots before the rami communicantes were given off, i. e. in the spinal canal. An intraspinal lesion was therefore diagnosed but the patient refused operation and left the Hospital May 19, 1913.

The patient returned to the Hospital July 4, 1913. The disability in the left arm had increased slightly and the atrophy was more pronounced; there was also slight atrophy in the right thenar eminence. The pains were severe and there was difficulty in walking. The pupils were the same as before. The knee jerks were exaggerated on both sides. There was an ankle clonus on the left side. Plantar irritation caused extension of the small toes but no movement of the great toes. The urine examination showed albumin and casts and the blood pressure was 180. There was edema of the feet and ankles and some dyspnea. The patient remained in the Hospital until September receiving treatment chiefly for the nephritis. The difficulty in walking gradually increased. It was considered very probable that there was something, probably a tumor, which was irritating the spinal nerve roots and gradually compressing the spinal cord. An operation was again advised but on account of the nephritis the prognosis was regarded as a little doubtful and the patient left the Hospital to try osteopathy.

She returned, December 11, 1913, for an operation. She was then totally paralyzed in both lower extremities and was unable to sit up. She had been in this condition for about two weeks. She had retention of urine, cystitis and probably pyelonephritis. There was no atrophy nor deformity of the legs. The knee jerks were exaggerated on both sides about

equally. There was ankle clonus and a positive Babinski reflex on both sides. The "defense reflex" was present in both legs. Pain sense was diminished in the legs, while tactile sensibility was relatively preserved. The conditions in the upper extremities were about the same as on her previous admission. The blood examination was negative. The urine showed albumin and casts and the systolic blood pressure was 205-210 millimeters Hg.

An exploratory laminectomy was done by Dr. C. B. G. de Nancrède, December 22, 1913. The spinous processes and lamina of the seventh cervical and first and second dorsal vertebrae were removed. The dura bulged greatly and showed no pulsation. The incision in the dura gave a gush of cerebrospinal fluid, apparently under considerable pressure. The spinal cord seemed small but otherwise normal. The incision in the dura was about one and a half inches long and at about the level of the first dorsal vertebra.

On December 23, her temperature was 100°. She said she felt well and had no pain. The examination gave the same findings as before operation, except that the Babinski reflex was less definite. On the 24th she had no pain. The knee jerks were less exaggerated and plantar irritation caused flexion of the toes. January 30, 1914 she was up in a wheel chair. She complained of pain at the site of the operation wound and down the arms especially if she sat up too long. Her legs were not strong enough to bear her weight but she could move them at all joints and they were gradually getting stronger. The knee jerks were very prompt and there was an ankle clonus on both sides. Sensation to touch and pinpoint seemed to be normal in the legs. The upper extremities were about the same as before the operation. There was no difficulty with micturition. She said that slight voluntary movement was first noticed in the toes about three days after the operation.

April 15, 1914, the patient said that she felt well except for some aching in the arms. An examination showed that the pupils were rather small but they reacted to daylight and also in accommodation. The extraocular movements were normal. There was apparently no reaction of the pupil on either side from stimulation of the neck. There was no enlargement of the thyroid, nor of the postcervical glands. There was a marked atrophy of the small muscles of the left hand, also considerable atrophy of the left forearm but no marked atrophy of the upper arm. There was slight atrophy of the small muscles of the right hand. She had a slight tremor in the finger to nose test, probably on account of the weakness. The grip of the right hand was fair, of the left hand nil. She could extend the fingers of the right hand but could not extend the two middle fingers of the left hand. She could flex and extend the left wrist but could not approximate the thumb to the fingers of the left hand. She had no trouble in putting both arms above her head. Flexion of the left arm was strong but extension was very weak. Extension of the right arm was also weaker than flexion. The biceps and triceps reflexes were present and prompt on both sides and about equal. She could move the lower extremities at all joints but the movements were weak. The weakness was about the same in all of them; no paralysis in any special groups; no localized atrophy. She was able to stand and could walk with assistance. The knee jerks were very prompt on both sides, perhaps slightly more so on the right than on the left. There was an ankle clonus on the right side, also on the left side. The Achilles reflexes were exaggerated. She said she felt pinpoint very sharply in both feet.

Case 2. An iron moulder, age 49 years, was admitted to the Hospital, December 30, 1913, complaining of girdle sensation, paraplegia, retention of urine and cystitis. His family and previous medical history contained nothing of importance. His first symptom was noticed about January, 1913, as a hot sensation between the first and second toes of the left foot. He later noticed various paresthesias in the left leg and about two weeks after the paresthesia appeared the right leg became weak, and about two months after that the left leg was also affected and he became unable to continue work. In August, 1913, he was examined by Dr. Safford, of Detroit, who noted that sensation in the legs was not disturbed but that his gait was spastic and he could only walk a few steps. At this time he began having difficulty in emptying his bladder. On his admission to the Hospital he had complete paraplegia with exaggerated reflexes and a positive Babinski reflex. There was a girdle sensation about the abdomen just above the umbilicus. He had complete retention of urine, also some cystitis. Sensation to pain and touch was lost in both legs and up to about the level of the umbilicus. There was no deformity of the spine and nothing abnormal in the head or upper extremities. The physical examination was negative. The blood count was normal. The urine showed albumin and leucocytes but no casts. The Wassermann reaction on the blood and spinal fluid was negative. The spinal fluid was very slightly yellow. There were seven lymphocytes per cubic centimeter. Pandy's reaction was very positive. Nonne Apelt, phase 1, was very positive; and the total amount of albumin was much increased. He was re-examined from day to day and no change noted except that the level of lost sensation seemed to be rising slightly and was near the tip of the xiphoid cartilage on January 14, 1914.

It was deemed advisable to do an exploratory operation to see if any pressure on the spinal cord was present and on January 16, Dr. C. B. G. de Nancrède removed the spinous processes and laminae of the sixth, seventh and eighth dorsal vertebrae. There was no extradural tumor. The dura was opened and the spinal fluid appeared to be under considerable pressure. There was some thickening of the dura and the arachnoid appeared milky. The spinal cord seemed very small, not over three millimeters in diameter. There was no visible pulsation either before or after opening the dura. He was transferred back to the Neurological clinic, February 2, 1914, and said he was feeling well. He had no difficulty in urination and no retention. He had normal sensation in passing urine. He could move the left leg at all joints. He could move the right ankle and the toes of the right foot but not the right knee. The knee jerks and Achilles jerks were very prompt but there was no ankle clonus and plantar irritation caused flexion of the toes on both sides. Sensation was not accurately tested but he claimed to be able to feel touch and pinpoint plainer in the legs than before the operation.

April 12, he was feeling well and had no disturbance in urination, no incontinence nor retention of urine or feces. He had a slight girdle sensation, at times accompanied by jerking in the legs. He said that he could stand by his bed but could not walk. He stated that the retention had disappeared four days after his operation and that he began moving his toes about one month after the operation. His legs were extremely spastic; any attempt at movement increased the spasticity so that movements were practically impossible. He could stand if he steadied himself with his hands. There was no atrophy nor deformity of the legs and the electrical reactions were normal. The knee jerks and Achilles jerks were exaggerated and there was spontaneous ankle and patellar clonus. The plantar reflex was present. The cremasteric reflexes were present. The abdominal reflexes were absent. There was some tremor of the hands on extension but otherwise the upper extremities were normal.

A lumbar puncture was done April 13, 1914. The pressure was low and after about eight cubic centimeters were withdrawn the flow ceased. The fluid was clear, light yellow color and on standing a few minutes became jellylike. Microscopic examination showed about six red blood cells and two lymphocytes in the fluid per cubic millimeter. Globulin and albumin were much increased. Adding 2 cubic centimeters to 1 cubic centimeter of Fehling's solution gave no precipitate but a strong purple color.

Derrien, Mestrezal and Roger (*Revue Neurologique,* 1907, No. 17) report a case similar to this one and were able to find twelve in the literature at that time. They suggested the name "Hemorrhagic Encysted Spinal Meningitis." The pathogenesis of the condition is undetermined but antisyphilitic treatment has not been beneficial and the injection of electromercurol or collargol has proved harmful—the medicament remaining at the point of injection. Repeated daily lumbar punctures have benefited two cases.

A somewhat similar condition of the spinal fluid may be found in spinal cord tumor especially in cases of diffuse sarcomatosis of the pia.

In both of these cases there can be little doubt that the condition actually causing the symptoms is a myelitis and from the history obtained of the gradual onset of the progressive character of the symptoms, it seemed likely that something was gradually compressing the spinal cord. No compression by bone or tumor was found at operation and it is quite possible that in both cases the compression was due to a local accumulation of fluid—in the first case a localized serous meningitis and, in the second, a hemorrhagic meningitis. In both cases, but especially in the first case, the relief of pressure by a laminectomy and opening the dura gave relief of some of the symptoms.

DISCUSSION.

Dr. Theophil Klingmann: Dr. Camp has covered the subject so thoroughly that there is very little to add. I may say, however, that the cases reported show very clearly that they are like many others that we see in which operative interference came too late. However, operation brings improvement and possibly cure if it be done early enough. The disability is due to changes in the spinal cord, the result of pressure.

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(1) A CASE OF CHANCRE OF THE LIP WITH EARLY INVOLVEMENT OF NERVOUS SYMPTOMS FROM SYPHILIS OF A FULMINATING TYPE.

(2) A CASE OF DERMATOSIS IN A PATIENT EXHIBITING MEDICAL, NEUROLOGIC AND PSYCHIATRIC FINDINGS.

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CASE 1.

I have taken the liberty of demonstrating two cases tonight rather than one. The first case is shown on account of the unusual localiza-

tion of the primary sore and on account of the fulminating character of the symptom complex which it illustrates. This man is 21 years old and enters the Hospital for a sore on the lower lip. If you inspect this sore you will note that he has a crusted lesion on the lower lip and at the same time a large tumor mass on the left angle of the jaw. The history of the case is that he contracted this sore four weeks ago. Within a very short time it took on the characteristics of induration and very soon it reached its present size. Now the usual period of incubation of the primary sore from the time of infection until the time it has reached its full development is about four weeks, and from this time until the secondary manifestations are shown or the secondary period takes place, varies from four to seven weeks. In this individual, however, there is present together with the primary sore and the adenopathy, a roseola and a papular rash over the body. There is a belief among medical practitioners that extragenital lues takes a much more serious course than does lues in which the primary sore is contracted on the genitalia. A priori, there would seem to be no reason for this. The reason is an apparent one. The extragenital sores are less frequently properly diagnosed and for this reason are less frequently treated from the outset, and the time lost in the early treatment influences the frequence of the late sequelae.

In addition to the secondary manifestations which are present in the primary period, this man has a distinct involvement of the nervous system. The lumbar puncture shows a marked lymphocytosis, positive Wassermann and increase in globulin and albumin content.

The etiology of a sore of this kind is usually osculation. It must be remembered, however, that extragenital sores of the lip may occur from mediate as well as immediate contact. A sore of this nature could easily occur from an infected drinking cup, from table ware, pipes and cigarette holders, as well as from genito-buccal contact. The apparent reason, I think, for the fulminating character of the disease in this case can be explained on anatomic grounds. There is much less resistance in the subcuticular structure of the mucous membrane than there is in the subcuticular structure of the skin. The glands are much more quickly involved and would seem more susceptible to the organism when the mucous membranes are involved in the primary focus, than when the primary focus is in the skin. It is interesting to note, in connection with the early involvement in this case that Dr. Stokes and I have found that 30 per cent. of all cases in the secondary period have, either with or without manifestations, central nervous involvement. This fact gave rise to the statement of Wassermann himself that the fate of every luetic patient was determined in the first year. Comparing 30 per cent. of all early nervous involvement with late nervous sequelae, we must conclude that the majority of these cases in which the nervous system is attacked early, undergoes a spontaneous resolution or resolution under treatment. And we may not perhaps be wrong in assuming that these cases in which the spirochaete remain, either because of some particular virulence of the organism, or because of insufficient treatment, or lastly—a point which is extremely difficult to determine—because of the relative susceptibility of the nervous capital of the individual, that these cases develop the late sequelae of lues. The question comes up in a case of this kind, is anything to be gained by destroying the site of the primary sore? I should say at once that nothing is gained at all by excision or cauterization of the primary focus where it is seen in a fulminating case of this kind. This is one of perhaps one hundred foci and to destroy it with any hope of amelioration would mean destroying all other foci. This patient has had arsenobenzol and it is hoped that he may make a speedy recovery without further nervous involvement under further treatment.

Case 2. The second case is one of more than usual interest on account of the fact that it led to a disagreement in the staff. Now we are particularly interested, in view of the dermatologic findings, in his neurologic condition. It has long been known that pruritic conditions react reflexly upon the nervous system. Patients with scabies, for example, in which the condition is not recognized, who suffer intensely from pruritus, are rendered extremely nervous and irritable, and prolonged neurasthenia can result from chronic pruritic conditions. It is also noted in cases in which there is functional nervous derangement, that dermatoses give rise to much more serious consequences than in patients who are normal. The French have described a distinct dermatosis to which they have given the name "neurodermitis"—a condition simulating lichen planus. I was inclined to regard this case as one in which, in a patient who was neurotic and who had a distinct neurologic condition, perhaps chorea developed from a perfectly banal dermatologic condition, lichenification. Dr. Holmes felt that this case was one of lichen ruber planus on account of the pseudo lichenification. The only way to determine this was to do a biopsy.

DISCUSSION.

Dr. John H. Stokes: One point of interest in connection with the case of primary lesion of the lip occurs to me. It is possible to make a laboratory demonstration of the identity of this lesion provided the examiner can use a dark-field miscroscope, sim-

ply by aspirating one of the glands in the satellite adenopathy in the neck, and examining the serum for the organism. I succeeded in this case in demonstrating large numbers of pallidae without difficulty. The procedure can be readily carried out with the ordinary hypodermic syringe and a fairly stout needle. The gland should be firmly fixed between the thumb and finger. When the needle pierces the capsule, the gland will of course move with the needle, which should then be twisted about until enough trauma results to make aspiration of some of the contents possible. The procedure is not painful. By aspirating the gland one avoids of course the necessity for making a differential diagnosis between pallidae and mouth spirochaeta which would be necessary in taking serum from the surface of the lesion. As a diagnostic resort, such a demonstration should be unnecessary to a keen observer, but its employment adds a gratifying sense of completeness to the examiner's study of the case.

The second case is one whose unusual interest is attested by the fact that Dr. Holmes estimated not less than ten different diagnosis to have been advanced to cover different phases of the patient's condition. From the dermatologic standpoint the boy's progress has been very satisfactory. Under bathing, bland local medication of an antipruritic character and the use of Fowler's solution in ascending doses the eruption is rapidly clearing up, even the more prominent papules on the thighs showing signs of involution. The boy perspires profusely at times and after each exacerbation of this trouble presents large numbers of miliary vesicles, especially over the back. The general mental condition seems improved under isolation and the boy is certainly very open to suggestion. The pulse has remained high, the heart sounds normal. In view of the difference of opinion on the diagnosis, of the skin condition, biopsy was taken from three groups of lesions presenting all the typical characters of the eruption, including the vesicles, and this material is demonstrated before you tonight. The pathologic picture is certainly not that of acute lichen planus. The round-cell infiltration of the papillary body, the acanthosis with marked proliferation of the interpapillary processes of the epidermis and root-like extensions downward into the corium are all lacking here. Instead there is marked atrophy of the Malpighian layer of the epidermis, and a fibroblastic infiltration of the papillary body, an increase in connective tissue such as is found in lichen simplex chronicus or neurodermitis. The section is through one of the typical lichenoid papules. The vesicle shown in the other section is of course scarcely diagnostic of the condition. It is very superficial and although the connection with the sweat gland duct beneath is not directly demonstrable, its presence at least lends color to the belief that this may be a sudamical or sweat vesicle, a view which I think Dr. Wile would not discountenance. The pathologic material, then, would identify this dermatosis as lichen simplex chronicus or neurodermitis and not as lichen planus.

Dr. John T. Holmes: Clinically the second case seemed to me to be very much like lichen planus for the following reasons: The eruption was of long standing and there was excessive pigmentation. It was exceedingly pruritic and on the thighs there were certainly small, angular, flat-topped papules. Before coming to the Hospital the case was diagnosed as lues and accordingly had been treated with mercury. Both mercury and arsenic are of value in causing lichen planus to involute and the vesicular elements found on the trunk might have been due entirely to this treatment. Of course there are quite a number of dermatoses that tend to clear up under treatment with arsenic, just as this case has. Finally the only way of settling the diagnosis is by the pathologic demonstration of sections of the papules, which may be seen under the microscope.

Dr. C. D. Camp: I saw this case only as a referred case and made no prolonged study of it. I think that probably most of the Society have observed while he has been in the room the typical choreiform movements of the patient. They are asymmetrical, irregular movements and might possibly be hysterical, but in my judgment they are too slow for hysterical movements. The latter are quick movements. One has to be guarded in this case because it is quite true that in some instances one finds chronic infections of one kind and another, or chronic intoxications giving rise to choreiform movements which are practically indistinguishable from Sydenham's chorea. The patient is congenitally a deviate, and, therefore, Dr. Wile's suggestion that the nervous manifestations may be simply a result of the skin irritation acting upon a congenitally predisposed individual is quite possible. Changes in the reflexes are common in Sydenham's chorea and maniacal attacks are not uncommon. They are generally spoken of as cases of chorea insaniens. I am inclined to believe that we are dealing with a case of Sydenham's chorea.

Dr. Harry Schmidt: This patient was referred to Medicine for examination. I could not obtain a history from him as he was apparently very dull and refused to answer questions. At the time I saw him he had no muscular twitching and there was a fine tremor of the hands and fingers. There was no exophthalmos but a very definite Von Graeffe. His pulse rate had been running between 120 and 136, his skin was warm and moist. He had no temperature. There was a brown pigmentation over the trunk, back and arms. The case was diagnosed as exophthalmic goitre, in spite of the fact that he had no exophthalmos, and no definite goitre. Dr. Hewlett saw the case later and concurred in the diagnosis of Sydenham's chorea. The most convincing symptom against Grave's disease is his apathy and dullness.

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(1) A CASE OF BILATERAL SPECIFIC DISEASE OF THE LABYRINTH WITH LEFT FACIAL PARALYSIS OF THE PERIPHERAL TYPE.

(2) A CASE OF OTITIC THROMBOSIS OF THE SIGMOID SINUS. WITHOUT SYMPTOMS.

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Case 1. I wish to present this case of specific disease of the labyrinth, which has very kindly been referred to me by Dr. Wile for investigation of the ear condition. The salient points in the history are as follows: The patient is a man twenty-four years old. The initial lesion occurred seven months ago and was followed by no secondary rash. Three months ago he received one injection of salvarsan and

following that took mercury pills for two months. For two months he has had tinnitus in both ears, more marked in the right. The hearing became affected about three weeks ago. He has had no nausea nor vomiting, but has had some little dizziness. Two weeks ago, he entered the Clinic of Dermatology, where the Wassermann on the blood and spinal fluid was found to be positive. He immediately received three grains of neo-salvarsan. Two days later (April 3) the left side of the face became completely paralyzed. This paralysis was still complete on April 7th, on which day he was first seen in the Clinic of Otology. Since the paralysis occurred, he has received two more injections of neo-salvarsan.

April 7th, on his first examination in the Clinic of Otology, he showed the following functional test:

A. B. R.		A. B. L.
	Convers.	
1 ft.	Whisp.	2½ ft.
	Noise Appar.	
	Hearing Tube	
	Weber	Pos.
Pos.	Rinne	Pos.
—9	Schwabach	—5
A. B. R.		A. B. L.
—24	Cl	—14
	al	
	c2	
—7	c4	+5
	Calton	
	Stenger	
Plus	Vertigo	Plus
Plus	Tinnitus	Plus
	Equil Dist.	
	Spont. Nystag.	
Slightly Reduced	Caloric Nystag.	Slightly Reduced
18″	Nystag. after turn.	15″
	Galvan. Nystag.	
0	Fistula Symptom	0

The Weber in the better ear, the positive Rinne, the decreased bone conduction, the lowered high limit, all point indubitably to an auditory neuritis, while the decrease in the vestibular irritability as shown by the caloric and turning tests, indicates the involvement of the vestibular branch, although to a less degree. There was a complete left sided facial paralysis. with loss of the sense of taste of the same side.

Following this examination, he received two injections of neo-salvarsan in the Clinic of Dermatology, and has improved steadily under this treatment, both as to his hearing and to his facial paralysis. His present hearing test is appended:

A. B. R.		A. B. L.
	Convers.	
3′	Whisp.	5′
	Noise Appar.	
	Hearing tube	
	Weber	pos.
Pos.	Rinne	Pos.
—7″	Schwabach	—5″
A. B. R.		A. B L.
Slightly	Cl	Slightly
	a1	
	c2	
Slightly	c4	Slightly
	Galton	
	Stenger	
	Vertigo	
	Tinnitus	
	Equil Dist.	
1° Rotary wild	Spont. Nystag.	1° Rotary wild
Normal	Caloric Nystag.	Normal
20″	Nystag. after turn.	20″
	Galvan. Nystag.	
0	Fistula Symptom.	0

The facial paralysis has almost disappeared. All voluntary movements are perfect, but in involuntary winking, one sees that the left eyelid is closed over the eye more slowly than is the case on the other side.

To me, the interesting points in this case are these:

First: This patient had an acute syphilitic auditory neuritis, was treated for it with neo-salvarsan, and is making a satisfactory recovery of his hearing. In the past, those cases of syphilitic auditory neuritis, treated with salvarsan, have become worse. Indeed, the results have been generally so disastrous to the hearing that a syphilitic involvement of the auditory nerve has been considered an absolute contraindication to the use of salvarsan. The reason for this is perfectly clear. The cochlear nerve is very loosely bound and if attacked by the syphilitic process, promptly becomes markedly edematous. If during this stage salvarsan is administered in the dose usually employed, the reaction is so great as to completely destroy the function of the nerve, or at least to cause enough swelling to bring about an atrophy from pressure against the walls of the bony cochlea. Dr. Wile has apparently avoided this destruction by using neo-salvarsan in very small doses until a definite therapeutic effect has been noted. With this point in mind, I think we may venture to try salvarsan again in the form of neo-salvarsan, even in cases of auditory nerve involvement.

A second point of interest in this case is that the lesion of the facial nerve can be de-

finitely localized in the labyrinth by the fact that the chorda tympani is affected on the corresponding side.

CASE 2. Otitic thrombosis of the sigmoid sinus very generally exhibits even in the early stages of the formation of the thrombus certain symptoms which point with more or less certainty to the presence of this condition, that it seems worth while to report this case of complete thrombosis, which exhibited no symptoms of the presence of the thrombus.

Harry S., fourteen years old, presented himself in the Clinic of Otology on account of trouble which he had been having with the left ear for the past four weeks. This trouble began with pain which lasted for a few days and was followed by rupture of the tympanic membrane and the appearance of a serous discharge. Since then he has had but slight pain in the ear, but has had considerable discomfort in the left side of the head ever since. The important points in his examination included drooping of the posterosuperior canal wall, perforation of the tympanic membrane in the posterior half with considerable bulging of the entire membrane and the appearance of a seropurulent discharge in the external auditory canal. Slight mastoid tenderness was present over the antrum. He was advised to enter the Hospital for operation, but disappeared from observation for ten days, at the end of which time he showed a uniform, tender, brawny, swelling beneath the tip of the mastoid. The ear condition was about the same, the white count was 13,800, with 74 per cent. polys. On the following day, a complete mastoid operation was performed. Retraction of the soft parts showed the mastoid process discolored and with many bleeding points. The mastoid process was of the large pneumatic celled variety and was everywhere filled with granulation tissue and pus. The bone of the sigmoid groove was destroyed. The sigmoid sinus was covered with a large mass of purulent granulation tissue, pressure upon which showed that there was bone underneath it. The sigmoid sinus was opened and found to be completely thrombosed from the knee to a joint just above the jugular bulb. Free hemorrhage was secured from above but not from below. Careful manipulation proved that the bone underneath the sinus was a part of the sigmoid groove and that the thrombosis had so distorted the sinus as to force it out of its natural bed and to allow this portion of the sigmoid groove, probably as large as the little finger nail, to become buried in the dura of the inner sinus wall. On account of the fact that the thrombus was not infected, it was not deemed necessary to resect the jugular. The operation was completed without incident.

Except for the fact that it became necessary later to evacuate a collection of pus in the neck the convalescence was uneventful. This case is reported simply in order to put on record another case of complete obliteration of the sigmoid sinus without any symptoms by which the observer could be led to suspect the condition.

DISCUSSION.

DR. UDO J. WILE: I am quite prepared to agree with Dr. Canfield that there are certain cases of cranial nerve disease in which salvarsan is definitely contraindicated. Such are the cases in which the nerves are primarily diseased before treatment, a case of deafness, for example, or neuro-retinitis, or optic atrophy. In such cases it is better to institute other forms of treatment before salvarsan is administered. These are quite different from the cases in which the cranial nerve involvement comes on during a course of treatment with salvarsan. Such cases constitute the so-called neuro-recurrences, which were supposed at first to be due to the salvarsan toxicity itself. In a personal communication with Professor Ehrlich last summer, I had these neuro-recurrences explained satisfactorily. According to Ehrlich all these cases are due to basilar meningeal involvement. If a small dose of salvarsan be given in such a case, a Herxheimer reaction is apt to occur at the site of the foramen and marked accentuation of the process occurs, causing a pressure of the nerve trunk in the foramen, and consequent partial or complete paralysis. With the second dose of salvarsan, however, in these cases, as in the one before you, this finally disappears; the Herxheimer reaction and meningeal reaction subside and the nerve disturbance at once clears up. Therefore in an early case of cranial nerve disease in secondary syphilis, one may be dealing, in the first case with a true neuritis, and on the other hand with nerve affection due to pressure from edema.

DR. C. D. CAMP: This case strikes me as being very interesting and unusual. It is the only case I have seen in which facial palsy presumably due to syphilis was caused by involvement of the facial nerve in the Fallopian canal. In most cases of facial paralysis due to syphilis a basal meningitis is the cause of the paralysis. The loss of the sense of taste indicates that the facial palsy is due to a local extension of a syphilitic labyrinthitis.

DR. A. J. LORIE: This case is extremely interesting on account of the rapid recovery from facial paralysis. When he was first examined, he had practically complete facial paralysis on the left side These patients recover, but not always as rapidly as this one.

The cases of eighth nerve deafness following the administration of salvarsan, may perhaps be due to the character of the eighth nerve. This nerve as we know is more or less embryologic in character being loosely bound and the fibers having considerable room in their sheath. Following infection by the spirochete, we get a certain amount of edema. This edema is increased as we know it is with the Herxheimer reaction. The nerve fibers swell, but as they are enclosed in a tight bony canal, there is always a liability of pressure necrosis.

The seventh nerve, while it runs in a bony canal also is a very highly developed nerve with a tight sheath, which does not permit of the edema and separation of fibers as does the eighth. This may account for the difference we find in the two nerves following the administration of salvarsan.

DR. UDO J. WILE: I wish to say that I still regard this patient as having basal meningitis. Before any of the symptoms of seventh

nerve palsy developed his spinal puncture showed a very definite lymphocytic increase and a very strong positive Wassermann. It appears to me that this case, notwithstanding that it is a Bell type of palsy, is still the extension of basal meningitis. In reply to Dr. Slocum's question I will say that the patient complained of burning and stinging in the affected eye.

Dr. Canfield (closing the discussion): I am able to agree with both Dr. Camp and Dr. Wile. With Dr. Camp I agree that this auditory nerve deafness is due to disease in the labyrinth and is not due to a basal meningitis. This fact is very clearly demonstrated by the functional tests. I am able to agree with Dr. Wile that the patient has a basal meningitis because the character of the spontaneous nystagmus supports this opinion.

FOUR UNUSUAL CASES OF STRABISMUS PRESENTED FROM THE STANDPOINT OF DIAGNOSIS.

George Slocum, M.D.

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The cases which are about to be presented have several features which are of interest from the standpoints of etiology and diagnosis.

Case 1. E. A., age 35 years, first entered the eye clinic about three years ago complaining of itching and epiphora in both eyes. At that time she was refracted and glasses were prescribed for astigmatism. Vision in the right eye 6/6, left eye 6/7.5.

March 10, 1914 the patient returned to the Hospital complaining of a drawing sensation in the left eye which had been present for about three weeks. Two weeks ago she suddenly noticed that the left eye had turned in. Diplopia was not mentioned by the patient but careful questioning showed that it was at times present. Patient says a transient diploplia lasting about two weeks was present about four years ago.

The amount of convergence, as measured by the Priestly Smith method, is 31 tangent degrees. Pupillary light reflexes absent, accommodative reflex present, excursions rather small. Pupil of the right eye larger than that of the left eye. Examination with prisms and Maddox rod gave an esotropia, convergent strabismus, varying from 31 to 42 degrees. Refraction shows the presence of one diopter of simple hyperopic astigmatism in each eye.

On March 30th the primary deviation measured by Priestly Smith method was 52 degrees, the secondary deviation 65 degrees.

The first point of interest this patient presents is the bilateral epiphora without nasal obstruction. Bilateral epiphora without nasal obstruction coming on without inflammatory symptoms is always strongly suggestive of a luetic infection, the pathology of the process in the nasolachrymal ducts being analogous to similar luetic processes in the periosteum and mucous membranes of the nasal passages. This symptom has been more or less prominent in this patient for the last three years.

The next point of interest is the absence of the pupillary reflexes, which of course strongly suggests tabes.

A paralysis of one or more of the extraocular muscles is always suggestive of a luetic infection. We have, therefore, three important and apparently related symptoms, epiphora, loss of pupillary light reflex, and paralysis of the external rectus. We were, therefore, not surprised to receive a report from the Neurological Clinic that there is a loss of the knee jerks and that the patient is suffering from tabes, nor was it any more of a surprise that the Clinic of Dermatology reported that she has a positive Wassermann reaction. The fundamental cause of her trouble may therefore be considered as established.

The differential diagnosis between a paralytic and spastic strabismus is usually not difficult. In spastic strabismus the excursions are equal in all directions and diplopia is nearly always absent. In paralytic strabismus diplopia, when present, increases as the patient looks toward the paralyzed muscle, and diminishes or disappears as the patient turns the eye into the

Figure 1. Case I. Showing primary deviation, fixing with normal eye.

Fig. 2. Case I. Showing secondary deviation on fixing with the paralyzed eye.

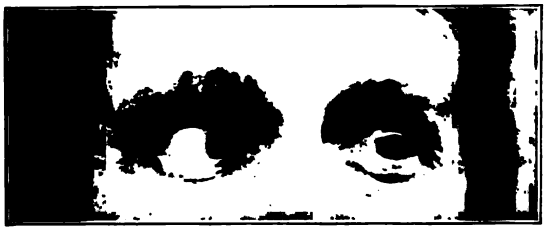

Fig. 3. Case I. Showing secondary deviation on attempting to turn the eyes to the left.

opposite field. In this case the excursion of the left eye in the direction of the paralyzed muscle is visibly limited until a strong stimulus is given, that is, when the limit of the nasal field for the right eye is reached and the patient continues to try to look toward the left, the left eye is able to turn practically to its normal extent. However, when this effort is made a convergent deviation of the unaffected eye follows which, as you see, is about 15 or 20 degrees in excess of that of the affected eye.

In this case diplopia is not a prominent feature possibly because the vision of the left eye is not as good as that of the right, possibly because a slight paralysis of the left external rectus may have persisted since the first attack four years ago and because the patient has learned to hold the head in such a position that no diplopia is present. When we observe this patient closely we notice that there is quite a marked tendency for the patient to turn her head toward the affected muscle in order that no demand for action may be made of this muscle and the eyes are thus permitted to assume the same position of parallelism as they take when the patient looks away from the affected muscle.

When diploplia is present in paralytic strabismus we are generally able to plot a diplopia chart. In taking a field of diploplia the affected eye is usually covered with a red glass so that the image having a false position is also red. By this means it is at once evident whether the false image is vertical or crossed or homonymous, that is, whether an adductor or an abductor, an elevator or a depressor is affected,

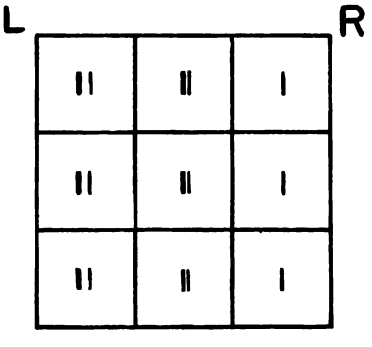

Fig. 4. Diplopia homonymous and present in the field of action of left external rectus; (heavy mark indicates left eye.)

and whether torsion is a feature of the diplopia, and if so, in what portion of the field the torsion is most pronounced. Having thus obtained the relative position of the false image we have only to remember the muscle which has the corresponding physiologic action and the diagnosis is complete.

Where more than one muscle or more than one eye is affected, the diplopia chart is less valuable and the diagnosis as to what muscles may be involved is often very difficult. In this case the patient fixes with the right eye and the left is crossed; the secondary deviation of the right eye is greater than the primary deviation of the left, the affected eye; the diplopia is absent on looking to the right, present on looking to the left; the diplopia is homonymous; while the left eye does not at first follow the movement of the right eye toward the left. After the limit of the nasal fluid for the right eye is reached the left eye is able to make a nearly complete left lateral excursion and a secondary deviation at once appears in the right eye which is greater than the primary. The strabismus is therefore paralytic and partial and is caused by a loss of power of the external rectus of the left eye.

In the management of this case, the lues should be properly treated and the general health and welfare of the patient be taken care of with such treatment of the tabes as seems to be advisable.

As to the local treatment, the patient's correcting glasses should of course be worn in order that the normal balance between accommodation and convergence may be maintained. Operation should be considered, only to be indefinitely postponed as these cases often completely recover. The patient may be encouraged to yield to the tendency to turn the head toward the affected muscle just enough to cause the diplopia to disappear. This will not only relieve the distressing symptoms such as nausea, vertigo, uncertainty, etc., which are often present, especially in deviations of a moderate degree, but it will have a tendency to stimulate any remaining power in the affected muscle, especially if the head is turned only enough to cause the diplopia to be nearly overcome by the position of the head, permitting the muscle to attempt the completion of the act of fusion and to prevent the tendency to the development of an amblyopia exanopsia in the deviating eye, a condition which nearly always does develop where there is a long continued loss of binocular vision from a continued deviation of one of the eyes.

Case II. J. W., age 20, came to the clinic March 30, 1914, in order that he might have his right eye straightened. The patient says his eyes were never injured and that his right eye has deviated outward since birth.

His vision is, OD counts fingers at 20 inches in the temporal field, O. S. 5/4. Pupillary reflexes, direct, consensual and accommodative are normal. His intraocular tension is normal. His right eye diverges about 60 tangent degrees by the Priestly Smith method. Ophthalmoscopic examination shows that the media are clear and the fundus is apparently normal in each eye. Both eyes are slightly hyperopic, the right somewhat more than the left. You will

notice when the patient follows a moving object with the fixing eye, the left, that his right eye moves in the same direction as the left and to the same degree in all portions of the field of fixation, that is, the squint is comitant. Further, on covering the fixing eye, the movements of the deviating eye are now apparently normal in all portions of the field, that is, the movements of the squinting eye are normal; then again, the primary and secondary deviations are equal. This case is therefore one of spastic exotropia or divergent squint.

Probably the most interesting feature of this case is the fact that the patient has a non-paralytic *divergent* strabismus associated with a *hyperopic* error of refraction.

The causes of spastic squint may be, (a) failure in the development of fusion power, (b) relative over stimulation of convergence by an accommodative effort made necessary by the presence of a marked hyperopia, or under stimulation in the presence of myopia, (c) a marked difference in the refraction of the two eyes, anisometropia, (d) amblyopia in one eye from congenital defect marked anisometropia, or from disease, (e) amblyopia or amaurosis in one eye due to opacities in the media or disease. Generally the refractive element in the etiology of strabismus is present in all cases of convergent squint no matter how many, or which of the other mentioned causes are present. In fact, always perhaps associated with undeveloped or partly developed fusion power, relative imbalance between accommodative and convergent stimulation is the main factor in a large majority of the cases of spastic squint. To explain this case, however, we must take another variety of muscular defect or error which does not usually enter into the production of strabismus, namely, the so-called phorias, sometimes called latent squint.

In routine examinations of the eye one discovers a large number of cases in which as soon as binocular vision is suspended, for example with a prism or a Maddox rod, one discovers a position of rest for the two eyes in which the visual axes do not point toward the same place, but in different directions, that is, the visual axes diverge or converge, or one axis points higher than the other. Such cases, not having any manifest deviation under normal conditions but showing deviations as just given, are said to have exophoria, esophoria or hyperphoria as the case may be. Now it is evident that when one eye of such a patient becomes injured or diseased, so that vision is no longer at all equal, the stimulus for fusion, that is, the effort to maintain the image on the corresponding points of the two retinae will no longer be made, the eyes will then tend to assume a position of rest, the previously existing phoria or latent squint will become manifest, and the eye will diverge if the previous condition were one of exophoria, converge if it were esophoria, or deviate upward or downward if hyperphoria were present.

Inasmuch as in this case, there is no marked refractive error, the strabismus is probably not due to relative over or under stimulation, nor can it be due to anisometropia; since the eye is to all appearance normal it is evident that the deviation is not caused by opacities of the media or by disease. There remain, therefore, two possible etiologic factors for consideration, first, a failure of fusion; second, a congenital amblyopia. As to the failure of development of fusion power in this case one can only say, we have no visible ocular defect, no marked refractive error, no anisometropia to explain the strabismus. We are, therefore, forced to conclude that the failure of fusion is not so much due to lack of development as it is to the amblyopia. If this were a case of acquired amblyopia, that is, one of amblyopia exanopsia, the amblyopia would follow one of the causes of strabismus which we have already ruled out, or it would follow as a result of a deviation for which no adequate cause has been found. It is true that a convergent squint might develop as a result of a hyperopia which has disappeared later during physiologic development, but this case has always been divergent. Of course it must not be forgotten that myopia and divergent squint are often associated but we have ruled out myopia. Are we not, therefore, justified in concluding that we have here one of those rare cases of congenital amblyopia in which fusion failed to develop, not because of any defect of a fusion center, but because no benefit would result if fusion did develop? Only one thing more is necessary and the analysis of the conditions will be satisfactory. If this patient had been born with a relatively perfect anatomic arrangement of the ocular muscles, both as to their innervation and as to their origin and insertion, the eyes might still have assumed a relatively normal position, but this was probably a case in which if in every other respect the eye had been normal, there would still have been an exophoria present. Given the exophoria, the congenital amblyopia has caused the development of a divergent squint and that too, notwithstanding the fact that there is a small amount of hyperopia, the tendency of which, other things being equal, is always toward the development of an esotropia. If on the other hand the latent tendency had been toward esophoria the resulting strabismus would probably have been convergent.

Cases of congenital amblyopia are rare. Worth reports only seventeen well authenticated cases in his book on squint. Other authors have occasionally reported such cases and in many, refractive errors are present to such a degree that they cannot be positively ruled out as etiologic

factors. It is rare indeed that a case is seen which presents such unique features as does this one.

The treatment of strabismus depends to so great an extent upon its cause or causes, and the method of treatment is so interwoven with the diagnosis that it is a matter of some interest to inquire into the best course of procedure in this case. First, we have decided that there is a lack of fusion power which we have no hope of establishing. Second, there is no error of refraction having an etiologic relation to the deviation; there is no anisometropia and for these two reasons the wearing of glasses would not improve the condition. Third, there is no removable cause for the amblyopia. Fourth, because of the age of the patient it is unlikely that the deviation could be corrected even if there was a refractive error or an anisometropia, the correction of which would establish a normal balance of stimulation and improve the vision. Fusion power can only be established in cases which are treated early, especially if amblyopia is an important feature.

It would seem necessary, therefore, to adopt some surgical means of correction. We have a choice of three operations for the correction of the divergent strabismus: One is a tenotomy of the external rectus muscle; a second is advancement of the internal rectus; a third is a combination of these. Tenotomy of the external rectus seldom gives an improvement of 10 degrees deviation, usually much less. Advancement of an internus may relieve a deviation of 15 or 20 degrees. On the other hand a combination of the two procedures often gives a very large gain. This case has a deviation of 60 degrees, therefore the combined operation is the one indicated. It is not at all unlikely that a similar operation on the other eye may be necessary before complete parallelism can be restored. In discussing the question of why an operation on the fixing eye could be done with benefit one must remember that this is a case of comitant strabismus, that comitant squint is spastic and that in spastic squint the over action is about equally divided between the associated antagonists, that is, between the interni in convergent, or between the externi in divergent squint. The mechanism is as follows, taking the present case of exotropia as an example: first, the spastic condition develops, in this case because of muscular imbalance; second, because of some one or more of the other causes, in this case a monocular congenital amblyopia, the eyes yield to the spastic impulse and diverge, the amount of divergence being equally divided between the two eyes; third, because of the fact that we must direct the visual axis toward an object in order to see it distinctly, one eye must be used for fixation, usually the better eye as in this case, and the deviation is made to appear to lie in one eye only, that is, in the nonfixing eye. Now as soon as a surgical correction of the deviation is done by an operation on the deviating eye, the necessity for fixation again divides any remaining error between the two eyes as before, and a further operation on the fixing eye will affect the mechanism of the deviation in the same way as did the former operation on the deviating eye.

Fig. 5. Case II. Showing deviation of amblyopic eye.

Fig. 6. Case II. Showing improvement obtained from the first operation.

Case III. C. R., age 38 years, referred to the eye clinic from the Neurologic clinic by Dr. C. D. Camp, March 29, 1914, where the patient was being treated for sacroiliac and sciatic rheumatism. The patient gave the following history:

When he was two years of age he was wounded in the right eye with a table fork. Since that time the right eye has turned out and the vision in O. D. has been poor.

His vision is as follows: O. D. counts fingers at 6 inches, O. S. 5/4. Pupillary reflexes, direct, consensual and accommodation are normal O. U. His intraocular tension is normal. His right eye diverges about 50 tangent degrees by the Priestly Smith method. External examination of O. D. shows a deep anterior chamber, iris flat, lens absent, lens capsule fills pupillary space excepting nasally, where a fundus reflex can be seen with the ophthalmoscope, but because of the smallness of the opening and the presence of capsular fragments (secondary cataract) no fundus details were obtained. Ophthalmoscopic examination shows that the fundus of O. S. is normal and that there is very little if any refractive error present.

Examining the patient in the same way as we did Cases I and II we find extraocular movements normal in every direction, the same relative position of the eyes being maintained in all portions of the field of orientation excepting that on accommodation for the near point, the divergence is appreciably lessened. The primary

and secondary deviations are equal. We have here therefore a second case of comitant divergent squint of much the same type as that of Case II, differing, however, in a part of the etiology and in the type of amblyopia. The difference in the etiology lies in the fact that in Case II the amblyopia is probably congenital, while in this case it is due to traumatic aphakia causing high hyperopia in O. D. and as a consequence very marked anisometropia complicated with a loss of accommodation in the right eye. It is probable that the determining factor of the divergence was, as in the other case, a latent divergent squint or exotropia.

The treatment of this case is like that of Case II. The question as to the advisability of the wearing of glasses for the correction of the monocular aphakia is one of considerable interest. Inasmuch as the focal distance of such a correction must be much greater than that of the intraocular lens of the other eye, the image on the retinae in the two eyes cannot be the same. A correction of an aphakic eye cannot supply the lost accommodation, therefore, while the perfect eye can accommodate for all distances up to the near point, the aphakic eye can only see at the distance for which it is corrected and change of focal distance can only be obtained by changing glasses. It would therefore be illogical to expect an aphakic eye to functionate for binocular vision with a normal fellow eye, and in actual experience such is found to be the case. For this reason, therefore, a correcting cataract lens is not prescribed in monocular aphakia where the vision in the other eye is functionally satisfactory.

As to the treatment of the strabismus the indications are the same as in Case II. We have here an amblyopic diverging eye, the character of the deviation being spastic or nonparalytic for which no treatment can be advised other than surgical interference for the improvement of the patient's appearance.

The choice of operation and technic to be followed are practically identical. As the amount of deviation is somewhat less there is more hope that an operation on one eye may be sufficient, although the chances are somewhat against this being the case.

The patient was transferred to the Clinic of Ophthalmic Surgery for operation March 31, tenotomy and advancement being done on O. D. two days later. The following photographs show the position of the eye before operation and the nearly corrected position after.

The question as to the best time for a second operation is of interest. Often these cases show complete restoration at the time of operation; during convalescence and for several weeks afterward the deviation often appears to be under corrected, later a secondary improvement sets in, until after a year or two the eyes often will have become parallel.

CASE IV. G. S., age 32. Patient entered the clinic March 5, 1914, hoping that his eye might be straightened. He gave the following history: Thirteen years ago his head was crushed by a log rolling over it; patient was unconscious for three weeks following this injury. At the time of the accident the right eye was seriously injured and both eyes bulged forward for sometime afterward. During convalescence fragments of bone were removed from the right side of his head. Since the accident, vision in the

Fig. 7. Case III. Showing deviation of aphakic eye.

Fig. 8 Case III. Showing improvement obtained by first operation.

right eye has been very poor; both eyes have been constantly convergent and only by turning the head to the left is the patient able to see well with the left eye.

His vision is O. D. 2/60, O. S. 6/7.5. Pupillary reflexes impaired especially in O. D. The patient's eyes are both strongly converged, elevation and depression present but limited; neither eye can be brought from convergence to the median line when the other eye is covered, and on making such an attempt with either eye the covered eye shows a marked increase of deviation (secondary deviation). The amount of convergence measured by the perimeter was O. D. 65 degress, O. S. 20 degrees.

Diagnosis: bilateral abducens paralysis probably from fracture of the base of the skull with injury of both sixth nerves either at the time of the accident or subsequently from hemorrhage, or from inflammatory reaction following the trauma.

The patient was referred to the Neurologic Clinic from which was reported a paralysis of both sixth nerves, right sided paralysis of the seventh and eighth nerves, probably from fracture of the base of the skull with hemorrhage.

The stereo plates taken in the X-Ray Department by Dr. Van Zwaluwenburg, failed to show definitely the position of the fracture, although some localized density was discovered

in the region of the squamous portion of the temporal bone.

Wassermann blood examination made in the Dermatologic Clinic gave a negative reaction. External examination reveals a scar of the cornea with anterior synechia and shallow anterior chamber, O. D. Other than the deviation, the appearance of O. S. is normal. On attempting to bring the left eye to the primary position the right eye shows a marked nystagmoid movement.

Ophthalmoscopic examination: O. D. Fundus reflex but no details. O. S. No fundus lesion, eye hyperopic with hyperopic astigmatism.

This case is entirely different from Cases II and III, which were spastic and divergent, and somewhat different from Case I, first, as regards etiology, in the one case lues in the other case trauma; second, in regard to the degree of paralysis, in the one case partial abducens and unilateral, in the other case total sixth nerve paralysis and bilateral, with involvement of the seventh and eighth nerves also. The first is a paralytic case which has a fair chance of recovery and which is certainly not operable, the fourth case is paralytic with, after thirteen years standing, no prospect of recovery unless operation is undertaken.

When an operation is performed on a nonparalytic or spastic squint, after the operation the eyes will move freely in all directions; on the other hand when a paralytic squint is operated no improvement in the functional activity results but the eye remains as fixed and none the less limited as to movement as before, notwithstanding any improvement in the position of the eyes that may be obtained; further, because all attempts to move the eye or eyes into the field of action of the paralyzed muscle will be associated with an extra stimulus to the opposite eye to move in the same direction, secondary deviation with paralytic strabismus will always be manifested in the field of action of the paralyzed muscle, consequently the eyes can be parallel or appear to be normal only when they are in the primary position. In this case the vision in the right eye is poor, consequently there will be a tendency to fix with the left eye and perhaps a corresponding tendency to the development of an unilateral squint due to a secondary deviation of the right eye.

The operation to be done in the fourth case must secure a correction of 85 degrees perimeter measurement which represents a much greater deviation than 85 tangent degrees. Consequently it will be necessary to secure the greatest amount of correction possible at a single time. To secure such a result, it will be necessary to operate upon both eyes, doing a combined tenotomy and advancement in each eye.

Fig. 9. Case IV. Showing amount and character of deviation.

Fig. 10. Case IV. Showing immediate improvement after the first operation. Tenotomy and advanceemnt of both eyes.

This operation was performed on this patient March 16, 1914. You observe that O. S. is now in its normal primary position and that already there is a tendency for O. D. to converge. For the further improvement of his appearance and in order that O. D. may be straight it will probably be necessary to do another operation on O. D. at some later time.

These four cases present three different types. Case I, nonoperable, paralytic, convergent strabismus requiring constitutional treatment, correction of refractive error, and patience. Case IV, operable, bilateral, paralytic, convergent strabismus requiring operation and correction of refractive error. Cases II and III, nonparalytic or comitant squint, the one congenital in origin, Case II, the other traumatic, anisometropia, aphakic, Case III, both requiring the same kind of operative treatment; neither having etiologic or influencing refractive error.

When a refractive error, such as hyperopia with convergent or myopia with divergent strabismus in a child, is under consideration the error of refraction must be determined and practically the full correction given, the amblyopia must be treated when present, and operation postponed, only to be considered after the age of eight or ten years in cases in which the eyes are not straightened when the glasses are worn, and in such cases, not until after the wearing of the correction at least a year or more.

These cases are reported by the kind permission of Professor Walter R. Parker.

DEMONSTRATION OF THE ELECTRO-CARDIOGRAPH.

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The department of Internal Medicine has recently acquired a string galvanometer for the study of diseases of the heart. Each heart beat produces electrical changes in the body. These may be recorded by attaching the electrodes of this very sensitive galvanometer to the arms or legs of the patient. The currents induced by the heart action pass through a single string of very fine silvered quartz wire, which is placed between the poles of a strong electro-magnet at right angles to the lines of force. The currents passing through the fiber case cause lateral deflections of it, which are approximately proportional to the strength of the current. The movements of the wire or fiber are recorded by projecting its image upon a moving film.

The instrument which is being used in the Department of Internal Medicine is Einthoven's latest model. In this instrument, the fiber is about 3.5 microns in diameter and has a resistence of from six thousand to ten thousand ohms. Its sensitivity can be varied by varying its tension. The usual degree of sensitivity employed is a deflection of the image of one centimeter for each millivolt. The speed of deflection is very great.

The instrument gives one the same sort of information as polygraph tracings, but the records are more easily obtained and more easily interpreted. The cardiac irregularities, especially, belong to the province of this instrument, and of these especially, auricular fibrillation and premature beats. It is possible to localize the origin of the latter very closely. Abnormalities in the conduction of impulses, which are sometimes impossible to recognize by polygraph tracings, as when due to lesions of the branches of the His bundle are easily recognized in the electrocardiograph tracings.

TRANSACTIONS
OF THE
CLINICAL SOCIETY
OF THE
UNIVERSITY OF MICHIGAN

STATED MEETING, MAY 20, 1914

THE PRESIDENT, R. BISHOP CANFIELD, M.D., IN THE CHAIR
REPORTED BY REUBEN PETERSON, M.D., SECRETARY

Reading of Papers

RADIOTHERAPEUTIC NOTES ON A CASE OF MEDIASTINAL TUMOR.

JAMES G. VAN ZWALUWENBURG, M.D.

Clinical Professor of Roentgenology, University of Michigan.

In the present stage of interest in radiotherapy, stimulated by the study of the radio-active bodies, there has arisen a huge mass of literature on the subject of procedures in carcinoma, to the neglect of certain other branches of X-Ray treatment resting on quite as solid a foundation of facts which have been accumulating for over a decade. The gynecologist has been attracted by the fact that carcinoma of the uterus is especially radio-sensitive, and, next to epithelioma of the skin, probably more amenable to treatment than carcinoma in any other location. It is to gynecologists that we owe the recent developments in technic which have made possible the administration of relatively large doses of X-Rays to deep-lying structures. Meanwhile, the demonstrated value of the ray in such conditions as Hodgkins, leukemia, tuberculosis, lymphadenitis, lymphosarcoma, etc., have been forced upstage and out of the limelight. It seems pertinent therefore, by a concrete example, to call attention to the effect of radiation upon a mediastinal neoplasm.

Mr. E. B. aged 28—was referred to the Hospital for diagnosis, with the complaint of pain in the left thorax, cough and swelling of the neck, face and arms.

In January, 1913, after an exposure, he first felt thoracic pain, which limited respiration, and radiated down the left arm. There was some cough without expectoration. The pain was not affected by position or aggravated by exercise. Four weeks before entrance, on October 15, 1913, after a lifting strain, his neck and arms became swollen and his condition much aggravated. The temperature was 99.8°, his pulse 120 and inspirations 24, on entrance; blood, urine and sputum examinations were negative and remained so except for a temporary flurry during an acute intercurrent infection.

On physical examination, he presented the signs of an interthoracic tumor with obstruction in the venous return flow from the upper extremities, slight exophthalmos, and beginning laryngeal paralysis. The cardiovascular signs of aneurism were absent and his Wassermann reaction negative.

On the 10th of October, while an out patient, he was fluoroscoped, and the diagnosis of mediastinal tumor confirmed. On the 16th, this finding was verified by stereoscopic radiograms, and a probable diagnosis of aneurism recorded. On the 25th of October, X-Ray treatment was begun with prompt improvement in the symptoms and signs.

The treatment was pushed to the tolerance of the patient's skin, at first on alternate days through five "ports of entry" on the "cross fire" principle. By November 16, 1913 he had received over twelve erythema doses (53 H.) of the hardest rays possible with our equipment, in ten sittings and twelve exposures. He was then discharged to return in two weeks.

He returned December 1, reporting that he had been feeling perfectly well, the only remaining symptom being a sense of pressure on hearty laughing. The subsequent course of treatment consisted of nine erythema doses in six sittings. The series was interrupted by a recess of three weeks for the holidays. During these three weeks his symptoms had returned to some degree and a comparison of the orthodiagram showed a relative increase of the shadow, especially to the left above.

During the next six weeks he received twenty-five E. D. in twenty sittings with a remarkable improvement in the plate and the orthodiagram.

On April 9th, he returned with renewed complaints, having fainted twice and having considerable pain and dyspnea. Treatments were resumed with a prompt disappearance of all signs. Since this time thirty-one E. D. have been given in fifteen sittings, and the patient is free from complaints.

This simple recital of the facts entirely fails to carry the impression of improvement which you gain from a clinical study of the case. The most striking feature is perhaps the disappearance of pain with the beginning of irradiation. This is, however, so common an observation in cases of malignancy, as to be the rule, and has invariably led to an over-estimation of the therapeutic effect of the ray. That an actual reduction of the size of the mass has taken place cannot be doubted from the evidence of the disappearance of venous congestion and the radiographic evidence. Superimposed tracings from plates and orthodiagrams uniformly demonstrate a reduction in size under treatment and an increase during the recesses.

Reports of improvement in sarcomata under radiotherapy are not very rare. Pfahler of Philadelphia has recently reported a series of sarcomata of the extremities without recurrence over a period of years. These are for the most part favorably situated.

Modern methods of intensive irradiation with carefully controlled dosage and quality of rays have not been extensively applied to this class of neoplasm, nor has a sufficient time elapsed to give us a fair idea of the effectiveness of such methods.

Naturally the aim of radiotherapy is the destruction of all the neoplastic cells in the organism and anything short of this must be ultimately futile. That this may actually be accomplished is shown by numerous isolated examples in the literature, that it is difficult follows from the comparatively small number that will stand the test of time or microscopic examination. Wide differences in radiosensibility evidently exist between similar growths in similar organs. Moreover, equally wide differences exist between different cells in the same neoplasm. Thus, some growths are absolutely refractory from the beginning of treatment, while others, after apparently doing well for a time, later progress in spite of the most vigorous treatment, sometimes with an enhanced rate of growth. The obvious interpretation of these facts is that after the vulnerable cells have been destroyed they are replaced by descendants of the resistant individuals, which, inheriting the resistance of their ancestors, entirely change the radiosensibility of the growth.

With reference to the case under discussion, we can only say that he has repeatedly reacted in a remarkable and unmistakable manner to the X-Ray. He has received no other medication during the entire period. He is now receiving the largest doses of the most penetrating rays at our command, and he has been living in comparative comfort since October. The mass has not entirely disappeared, in fact appears to be about stationary at the present time. Three things may happen in the future, the tumor may become refractory, metastases may develop, or a cure may result, and in about that order of probability. The fourth alternative of the establishment of a condition of equilibrium between the destructive and the constructive tendencies may be dismissed, since the repeated application of the ray to other structures is certain to result in serious damage of some sort. Indeed, the tolerance of the skin places a very definite limit to the aggregate amount of X-light that may be given with impunity. What that limit is we do not know nor are we certain that we shall know when we have exceeded it. In the meantime, we shall continue to apply the rays as long as we dare, for we dare not quit.

PITUITRIN IN OBSTETRICS, WITH AN ANALYSIS OF FORTY CASES.

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It will always be the tendency for the practitioner of medicine to greet with enthusiasm any new preparation that may give him a certain amount of control over two very uncertain factors in obstetric practice, namely, the time of onset of labor and the strength and regularity of uterine contractions. Dale, in 1905, was the first to show experimentally that extracts of the posterior lobe of the pituitary body markedly influenced uterine contractions. It remained, however, for Bell in 1909 first to take practical advantage of this fact and apply it to his obstetric practice. Since this time extracts of the pituitary body have been marketed by various pharmaceutical houses. For obstetric purposes these preparations have been prepared in liquid form in ampules and in ounce vials, each cubic centimeter representing from 0.1 to 0.2 grams of the fresh posterior lobe. The preparation of Parke, Davis & Co., "pituitrin," has been used in all cases cited in this paper, one cubic centimeter being equivalent to 0.1 gram of the fresh gland.

Administration and Dosage.—It was found that the best results are obtained by intramuscular injections as the effect is likely to be delayed if given subcutaneously. It should also be remembered that administration by mouth should not be employed as the digestive juices destroy the activity of the preparation. The

question of proper dosage has been a matter of some debate, the German investigators using large doses, at times as high as a gram as an initial dose with apparently no ill effects. In this country Humpstone recommends 0.4 grams (4 cc. pituitrin) as the initial dose, repeated every twenty minutes for three doses when necessary. Edgar also says that for decided action 0.4 grams is usually required as an initial dose. On the other hand, Hofbauer and others conclude that 0.1 grams is sufficient in most cases and that in many cases 0.05 grams will have the desired effect. It has been our experience that from 0.1 to 0.15 grams will produce the required result in most cases, and that this dose may be repeated if necessary twice or three times. Occasionally a patient will fail to respond to repeated doses of pituitrin. This may, in some cases, be due to the fact that the preparation is old and inert but the fact remains that even with absolutely fresh pituitrin at times the desired results are not forthcoming. The action of large doses of pituitrin during the first and second stages of labor is, in our opinion, comparable to that produced by ergot, inasmuch as the contractions are so rapid that in reality a tetanus uteri is produced.

Induction of Labor at Term.—The use of pituitrin to induce labor at term has not, in the hands of most observers, been at all successful, and at present it is quite generally conceded that the results are very uncertain. Our experience is tabulated below, all cases being at or over term.

PITUITRIN TO INDUCE LABOR AT TERM.

Case No.	Dose cc.	Interval mins.	No. of doses	Results
III	1	20	3	None
VI	1	25	3	None
VII	1	25	8	None
XI	1½	15	2	None
XIV	1½	15	2	None
XV	1½	15	2	None
XVIII	1	15	3	None
XIV	1	15	3	None
XXXIII	1½	30	2	None
XXXIV	1½	30	2	None
11	1 (Pains began in 8 min. and continued until delivery)			Good
V	1	30	2	
	(6-8 painful contractions after the first dose. No result after the second dose)			

From the above table it will be seen that of twelve patients given pituitrin with the idea of inducing labor, ten showed no result from the injections, one had a few pains but did not go into labor, and in one, labor began eight minutes after the injection of one cubic centimeter of the preparation. In only one case was the desired effect obtained, that is, in Case II. This patient was due February 3rd, and the hypodermatic injection of one cubic centimeter of pituitrin was given the morning of February 5th. Lightening had occurred ten days previously but the patient had no signs or suggestions of beginning labor. In none of the patients was any ill effect noted following the administration of pituitrin.

In the First Stage.—In all our cases, aside from those in which we attempted to induce labor at term, pituitrin has been given only in the presence of sufficient indications and has not been used simply as a means of hastening normal labor. If this plan is carried out but few cases will require the preparation in the first stage. Serious ill effects have been reported from time to time from the injection of pituitrin in the presence of a partially dilated cervix. Herz reports a case of uterine rupture after the injection of one cubic centimeter of pituitrin, with the cervix dilated to the size of only two fingers, tetanic contraction ensuing in twenty minutes, and concludes that pituitrin should not be given in the presence of an insufficiently dilated cervix. Rieck reports a case of tetanic contraction requiring craniotomy to deliver the child. Heil and Mackenrodt both record cases in which cervical as well as uterine contractions occurred after the administration of pituitrin in the first stage of labor. It is justifiable to give pituitary extract in the first stage only in exceptional cases, never as a routine. The following case may serve to illustrate an exception.

CASE XXV. Primipara, normal pelvis. Position S.L.A. The membranes had ruptured at the beginning of labor, which had continued for thirty-one hours. The pains throughout had been weak and inefficient. Morphine sulphate, grains one-fourth, was given hypodermatically with the hope that after a rest the pains would become stronger. The pains, however, after morphine, continued weak and the patient was becoming very tired. Rectal examination showed the cervix three-fourths dilated, and easily stretched to the pelvic wall. The fetal heart was in good condition. One and one-half cubic centimeters of pituitrin were administered. In six minutes the pains had become strong and regular and the child was born spontaneously in forty minutes from time of injection.

In the Second Stage.—It is in the second stage that the best results are obtained with pituitrin. The following table gives the results of our experience.

Nineteen cases were carefully observed in all. Of these fourteen patients delivered themselves spontaneously after pituitrin in the presence of sufficient indications for its use, which in twelve cases were weak and inefficient pains and in two cases moderately contracted pelves. Thirteen of the fourteen cases were primiparae and in many of these there was sufficient indication for low or mid forceps before the pituitrin was given. Some idea of this can be gained by an inspection of the following table. That pituitrin

Case	Length of Labor before Pituitrin Hrs. Min.	Length of Labor after Pituitrin Hrs. Min.	Length of 2nd stage after Pituitrin Min.	Dose in cc.	Time to act Min.	Pelvis	Para	Remarks
Case 3	17° 25	1° 40	30	1	5	Normal	1	
Case 4	11°	4°	Low forceps	1	5	Normal	1	Low forceps for fetal indication.
Case 8	32°	3°	Mid forceps	1 dos. 3	No result	Normal	1	No result from pituitrin
Case 9	22°	2° 30	Mid forceps	1	5	Normal	1	Mid forceps for fetal indication
Case 10	4° 25	2° 30	35	1	6	Normal	1	
Case 12	27°	1° 40	15	1	4	Normal	1	
Case 13	23° 15	1° 15	15	1	5	Simple funnel	3	Bisischial diam. 8 cm
Case 16	8°	1° 45	30	1½	3	Normal	1	
Case 17	32°	3° 50	25	1½	5	Flat funnel	1	Ext. conj. 17.5 cm Bisischial 7.5 cm
Case 20	8° 55	1° 55	1°	1	10	Normal	1	
Case 22	16°	1° 50	46	1½	6	Normal	1	
Case 23	14°	2°	8	1	3	Normal	1	
Case 24	8° 30	1° 40	30	1½	5	Normal	1	
Case 26	3° 30	1°	38	1 dos. 2	10	Normal		
Case 27	17° 25	1° 40	30	1	6	Normal	1	
Case 28	19° 20	1°	20	1	7	Normal	1	
Case 29	67° 40	30	20	1½ dos. 2	5	Normal	1	
Case 31	15° 20	20	Version and Extraction 1	1 dos. 2	5	Normal	2	Version and Extraction for fetal indication. No result from pituitrin.
Case 37	8°	1°	No result	1 dos. 2	No result	Normal	1	No result from pituitrin.

markedly shortened the course of labor, and in many instances rendered the forceps operation unnecessary we cannot doubt when we consider that;

(1) The average length of labor before pituitrin was 19 hours 2 minutes.

(2) The average length of second stage before pituitrin was 1 hour 32 minutes.

(3) The average length of second stage after pituitrin was 28 minutes.

Furthermore the average dosage to effect delivery was one and three-sevenths cubic centimeters and in only one case were two doses of one and one-half cubic centimeters required, while in nine cases one cubic centimeter was sufficient for spontaneous delivery. The average length of time elapsing from the administration of pituitrin until the establishment of steady pains was 5 minutes 42 seconds, the shortest time being three minutes, the longest ten minutes. In the light of these findings we are forced to disagree with Humpstone, Edgar and others who advise a large initial dose, as, in our experience, one to one and one-half cubic centimeters have been amply sufficient. Still further we have found that cases which did not react at all to small doses (1 to 1½ cc) also often fail to react on repetition of the dose two or three times at frequent intervals. (See Cases, VIII, XXXVII, XXXI).

In some cases the pains were increased only in intensity and duration, in others they were markedly increased in frequency as well as in duration. No difficulty was experienced in controlling the head under obstetric anesthesia. It is our belief that pituitrin should not be given during the second stage until all preparations for delivery are made, as labor may terminate very quickly. (See Case XXIII). The results in two cases with slightly contracted pelves were most gratifying, both patients being delivered spontaneously 15 and 25 minutes respectively after one dose of pituitrin. (See Cases XIII and XVII).

Patients, IV and IX, were given pituitrin after very slow advance of the head during second stage; in both cases strong pains with some advance of the head occurred in five minutes but on account of the fall of the rate of the fetal heart, low forceps was done in the former and mid-forceps in the latter. It is probable that in the presence of no fetal indication both patients would have ultimately delivered themselves. As it was, Case IV was undoubtedly changed from mid to low forceps, and Case IX from high to mid-forceps by the use of pituitrin. From a study of these cases it would seem that pituitrin can well be used as an adjunct to the forceps operation with the idea of making operative delivery easier.

Three patients, VIII, XXXI and XXXVII showed no results after the administration of the preparation, patient VIII being given three doses of one cubic centimeter each and patient XXXI and XXXVII being given two doses of one cubic centimeter each. In each instance the

pituitrin was fresh, the patient free of fever and the injection given intramuscularly.

In Abortion.—In two cases pituitrin was given in inevitable abortion at the sixth month.

CASE I. Age 23, Para. 11. Normal pelvis. Position R.O.A. Six months pregnant.

Patient began bleeding rather freely at midnight. Pulse rose to 100. Fetal heart could not be heard. No quickening for past two days. Patient put to bed but was having no pains. Bleeding continued until 10 P. M., when vagina and cervix were packed with gauze. The cervix was dilated to admit about three fingers. After packing, the pains began irregularly. Pituitrin one cubic centimeter administered and repeated twice at intervals of twenty minutes with slight increase in pains five to six minutes after injections but not enough to cause expulsion.

CASE XXI. Age 25, Para. 7. Six months pregnant.

Patient entered Hospital in labor six hours. Examination showed pregnancy about six months, cervix dilated to admit three fingers; prolapsed, non-pulsating cord. The pains continued intermittently for an hour and finally stopped. Pituitrin one cubic centimeter was given and in six minutes the pains were strong and regular, a six months dead fetus being delivered in one hour.

In Case I the results were practically negative, while in Case XXI they were all that could be desired. It must be remembered, however, that in Case I while the cervix was dilated to admit three fingers the patient had had no labor pains, while in Case XXI with the same amount of dilatation pains had been present for six hours. Authorities seem to agree that we can expect no results from pituitrin in the induction of abortion, but that once started the clinical course of the latter may be shortened by pituitrin.

In Postpartum Hemorrhage.—In the treatment of postpartum hemorrhage the results are good but not better than those obtained by the use of ergot. Repetition of the dose is often required. We have noticed that the action of both pituitrin and ergot is augmented by previous injection, with the former of ergot, and with the latter of pituitrin. This has been illustrated by several of our cases in which pituitrin was given with apparently no effect but immediate contraction followed the subsequent injection of ergot, and vice versa.

In Cesarean Section. — Case XXXVI. Pituitrin was given in one case just before making the incision for abdominal Cesarean section. The uterus began to contract almost immediately. After delivery of the child the contractions were so strong that the posterior uterine wall and placental site were forced into the incision in the anterior wall. This greatly hindered the removal of the placenta and membranes and rendered the placing of the uterine sutures somewhat difficult. There was, however, very little hemorrhage. The child was rather badly asphyxiated but was finally resuscitated. As the patient was not in labor and the abdomen was opened under primary ether anesthesia it would seem that the asphyxia neonatorum was probably due, as suggested by Edgar and others, to compression of the placental site with coincident hypercarbonization of the fetal blood. Pituitrin, then, if used in Cesarean section as a substitute for ergot should not be given until after delivery of the child. Even then strong contractions may interfere with the suturing of the uterine wall.

Pituitrin and Blood Pressure.—In 1895 Oliver and Schafer showed experimentally that injections of extracts of the pituitary body were followed by rise in blood pressure and drop in pulse rate. In 1898 Howell demonstrated that it was the posterior lobe that possessed this property. Since that time investigators have fairly well agreed that clinically also such injections of extracts of the posterior lobe are followed by rise of blood pressure and slowing of the heart rate. This is undoubtedly true in some, perhaps in the majority of cases, but it has been our experience that rises in blood pressure and drop in pulse rate do not always follow injections of pituitrin. Cases XXXIV and XXXIX, illustrate what is usually supposed to occur. Cases XXXIII, XXXVIII, and XL give contradictory findings.

EFFECT OF PITUITRIN ON BLOOD.
Pressure and Pulse Rate.

Case	34		38		33		39		40	
	BP.	P.	BP.	P.	BP.	B.	BP.	B.	BP.	B.
Before	116	72	110	100	120	80	102	92	126	100
After 5	136	64	110	120	138	92	106	80	120	104
After 10	136	64	90	120	138	94	104	88	110	112
After 15	130	68	98	112	134	92	102	92	120	116
After 25	124	70	105	100	130	90	102	92	120	106
After 35									120	100

In Cases XXXIV and XXXIX the blood pressure rose after pituitrin, although the rise in Case XXXIX was so small as to be negligible, while the pulse rate was slowed in both cases. In Cases XXXVIII and XL there was an actual fall of blood pressure and the pulse rate was increased; exactly opposite results from what we would expect from the literature, while in Case XXXIII there was a rise in blood pressure but a corresponding rise also in the rate of the pulse. The results from pituitrin as regards increase of blood pressure, therefore, are not at all constant, and in some cases there is an actual fall in pressure.

Pituitrin and Urination.—Diuresis after pituitrin was noticed by Dale, Bell, Howard, Ott and others and seemed to be secondary to a rise in blood pressure. Loeb states that a

second dose of pituitrin fails to change the blood pressure but causes a marked diuresis. He therefore concludes that pituitrin has a specific action on the kidney outside of that on the blood pressure. However, a diuresis alone is insufficient to account for the reports of Quigley and others to the effect that postoperative and postpartum catheterization are rendered almost unnecessary after pituitrin. This can only be explained by the effect on the involuntary bladder muscle itself. From our series we are not justified in drawing definite conclusions but it is significant that of twenty-three patients given pituitrin during labor catheterization was necessary postpartum in only four instances, and in one of these (Case VIII) we failed to get results from pituitrin in the second stage. When we consider that the patients were primiparous in all but two instances, that labors were difficult in most cases and that there were four operative deliveries the percentage of patients requiring catheterization would seem small.

Untoward Effects.—We are not prepared to agree with those who state that the use of pituitrin is never followed by ill effects. Among our cases, III, XVI and XXXVI were followed by marked asphyxia livida in the child. All children were subsequently revived. It is probable that this is due, as has been mentioned previously, to severe compression of the fetus, particularly of the head and to hypercarbonization of the fetal blood from constriction of the placental site. Premature separation of the placenta occurred in none of our cases, neither did we find severe postpartum hemorrhage more likely to occur. We have not seen tetanus uteri and think it not probable, provided a small initial dose is given, although in some cases the pains come in quick succession. Rupture of the uterus is not likely if the cervix is dilated and there is no serious obstruction to labor.

In four cases, XXXIV, XXXVIII, XXXIX and XL, the patients complained of feeling faint very shortly after injection. The lips became cyanotic and there was a cold sweat over the brow and extremities. Patients XXXVIII, XXXIX and XI also complained of nausea, while in case XL there was moderate headache and irregular pulse. Heaney reports the same experience with one of his cases.

Conclusions.—In conclusion we may say that:

(1) Pituitrin is best administered intramuscularly.

(2) The initial dose should not exceed one to one and one-half cubic centimeters. Large doses during labor are equivalent to ergot and should not be given.

(3) In induction of labor at term the results are not satisfactory.

(4) In the presence of an undilated cervix pituitrin should be given only in exceptional cases.

(5) The best results are obtained in the second stage of labor.

(6) In an occasional case the preparation is apparently inert.

(7) It should not be given in the presence of serious obstruction to labor.

(8) In moderately contracted pelves and especially in outlet contraction the results are good.

(9) The forceps operation may often be averted or rendered easier by the proper use of pituitrin.

(10) In Cesarean section pituitrin should not be given before delivery of the child.

(11) The effects on pulse and blood pressure are not constant, but pituitrin should not be used in conditions associated with high blood pressure.

(12) Urination after delivery seems to be facilitated.

(13) The administration is sometimes followed by untoward symptoms.

(14) In postpartum hemorrhage the results are not better than those obtained by the use of ergot.

(15) Pituitrin has no place in normal obstetrics, and should be given only in the presence of sufficient indication, e. g. inertia, moderately contracted pelves, etc.

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REPORT OF (1) A CASE OF LYMPHANGIOMA CIRCUMSCRIPTUM. (2) A CASE OF LOCALIZID SCLERODERMIA.

UDO J. WILE, A.B., M.D.
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The case which I wish to present this evening is one of unusual interest and one of extreme rarity. It is the second case of its kind to have occurred in this clinic and one of the very few which it has been my opportunity to see and study. The lesions, as you see them, occur on the side of the neck. They appear in the form of split pea sized, translucent lesions, in which there is fluid. Over the surface of most of them you will note the presence of dilated bloodvessels, giving at first glance the impression that hemorrhages had occurred into the fluid content of the lesions. The lesions are distinctly grouped. Attention is called to the fact that there is no inflammatory reaction near or about them. Just above the group of lesions there are to be noticed a few depressed scars. These the patient states are the result of burning with carbolic acid, which was applied a number of years ago in the hope of destroying the condition.

In the differential diagnosis we have to consider herpes zoster, herpes simplex and the condition under discussion, lymphangioma circumscriptum. The absolute absence of inflammatory reaction and the apparent quiescence of the lesion, its duration over many years, unchanged, easily serve to differentiate it from either herpes simplex or herpes zoster.

The varicosities of the superficial lymph vessels and spaces are rare forms of tumors, as in this case, they are usually pearly or pinkish red, thick walled vesicles, many of which have minute telangiectases in association with them, and in many of which there may even be true angiomata of the cavernous type. Histopathologically one finds in such cases dilatation and new growths of the lymph channels, which appear as large spaces in the cutis extending up into the epidermis, causing a pressure atrophy of the latter, these spaces all being lined by endothelium. Spontaneous rupture may give rise to continuous leakage of lymph, but unless the growth is radically excised, simple interference or excision into the lesions gives rise to recurrences. We have decided in this case, at the patient's request, to remove the growth by excision, which offers the best cosmetic result for the patient and at the same time offers an opportunity for pathologic study of a rare condition.

Case 2. Localized Sclerodermia.—The second case which I wish to present is one again in which the differential diagnosis is both important and difficult. The patient presents over the skin of the right breast a firm, ivory white, indurated patch. This, as you will note, is rather irregular on the border and the surface is somewhat glistening. It is distinctly lardaceous to the palpating finger and stops rather abruptly at its free margin.

The lesion resembles, I think, somewhat closely the infiltration that occurs in the skin from breast carcinoma. There are many features on close examination which speak against this diagnosis. In the first place I should like to call attention to the fact that neither the nipple nor the areola is involved in the disease process. The lesion, as you note, completely encircles both the areola and the nipple, without, however, in any way involving them. There is also no involvement of the deeper breast tissues and there are no enlarged glands in the axillae. The mass is painless and there is complete absence of any inflammatory reaction.

The case is presented to you as one of typical morphoea, or localized sclerodermia. These patches are usually found anywhere on the body. Their etiology is obscure and their pathologic change is like that of true sclerodermia, principally associated with vascular obliteration. Dr. Stokes is at this moment studying the histopathology of morphoea this case being the third, which we have had the opportunity of studying during this past year.

The lesions usually start as small, indurated, ivory white patches with a distinct hyperemic border. They may disappear spontaneously and when this occurs they are usually followed by atrophy of the skin involved. The patches may be multiple or single. In my experience the lesions have more frequently been two or three in number. Therapeutically there is nothing which seems to influence them, nor is there any marked indication for treatment as the disease seldom carries an unfavorable prognosis with it, so far as life is concerned. This of course distinguishes it from the generalized form of sclerodermia.

REPORT OF TWO CASES OF AMEBIC DYSENTERY.

HARRY BURKE SCHMIDT, M.D.
(From the Department of Internal Medicine, University of Michigan).

The first patient, Mr. T. T., age 38, publisher, married, American, entered the University Hospital on March 15th, 1914, complaining of weakness, flatus and recurrent attacks of diar-

rhea of fifteen years duration. The family and personal history are negative. He has been in St. Louis, Mo., for a few days, Jacksonville, and St. Augustine, Florida for ten days, otherwise has always lived in Michigan. The present illness began fifteen years ago with nausea after eating. This lasted for a month at which time he was very nervous and overworked. He vomited occasionally. There was an insidious onset of diarrhea a year later and since this he has never had a formed stool. The stools have never been clay or tar colored. He has never noticed any pure blood in the stools, but considerable mucus. His appetite has been more or less capricious, though there is no history of indigestion. He has not been indisposed enough to go to bed. He has lost fifteen pounds in the last fifteen years. The physical examination is negative. There is nothing seen in his rectum to explain his trouble. On examination the stools are of a yellowish fluid consistency with some undigested food particles and considerable mucus. No microscopic blood was observed. The occult test has been repeatedly positive. Microscopic examination disclosed swarms of trichmonas intestinalis, a few red blood cells and three ameba with very rapid ameboid motion. One of the organisms was observed for a considerable length of time. It was not over sixteen microns in diameter; the movement was progressive and very rapid during which the ectoplasm and endoplasm could be easily distinguished. The organism finally came to rest, at which time the nucleus could be discerned as a small refractive body with an apparently thick capsule. The organism at rest was perfectly spherical and the ectoplasm and endoplasm could not be differentiated; there were many fine granules which began to circulate first in one direction and then in an opposite direction about the periphery of the cell. At this stage the observation was discontinued. At no time were any red blood cells seen in the ameba. Stomach, urine, blood and blood pressure were negative.

The patient was placed in bed on a finely divided diet with emitin hydrochloride, hypodermically, one-sixth of a grain, three times a day. Under this treatment his stools have become formed, and the mucus has entirely disappeared. The patient was discharged May 19, 1914, apparently well.

Case 2. The second patient,, Mr. L. M. age 29, American, single, entered the Hospital on March 30th, complaining of bloody diarrhea. His family and personal history are negative. He has never been out of the state of Michigan excepting for a few days in Windsor, Canada. The present illness began August 15, 1913 with a sudden onset of bloody diarrhea. His previous health had been good. Since this time he has had from five to six bloody stools a day accompanied by griping pain. During this attack he had no fever. After two months of rest in bed he lost sixty pounds. Under further treatment he regained this weight and became apparently well. The second attack began March 15, 1914, the complaint being the same as before with the exception that he has had an afternoon temperature each day. The physical examination is negative. Examination of the blood shows 3,720,000 red blood cells, 19,200 white cells and 65 per cent. hemoglobin, 75 per cent. polymorphonuclears, with 5 per cent. eosinophiles, 20 per cent. mononuclears. The urine and blood pressure were negative. The rectal mucous membrane has a red beefy appearance with numerous pin point bleeding spots, no ulcers being seen. The stools are of a fluid consistency and of a dark red color. There is considerable mucus. Microscopic examination shows numerous red blood cells, large numbers of ameba with slow ameboid motion. The organisms while at rest have a relatively large nucleus with a coarse granular endoplasm. The ectoplasm is not made out. However, the ectoplasm could be seen during the movement. No red blood cells were seen in any of the organisms. A diagnosis of amebic dysentery was made in this case, because of the ameba found in the stools and because no other condition could be found to explain the symptoms. Tubercle bacilli were looked for but none found. From the description of the above organism one would be inclined to include it under the nonpathologic entameba.

No cultures nor stains were made for the purpose of differentiating the organisms. It takes a trained biologist to be at all sure of the classification of these organisms, but in any given case of unexplained diarrhea with ameba in the stools, it would be advisable to treat the case as amebic dysentery.

The use of emitin hydrochloride in amebic dysentery has been wide spread in the past year or two. Many good results have been reported. As much as four grains per day has been given without untoward symptoms. Our first patient apparently had a very good result from this treatment. The improvement in the second case has been almost nil, about the only change to be noted being the diminution in the amount of blood, and this may be explained by the fact that emitin causes tonic contraction of nonstriated muscle and constriction of the arterioles.

TRANSACTIONS
OF THE
CLINICAL SOCIETY
OF THE
UNIVERSITY OF MICHIGAN

STATED MEETING, JUNE 10, 1914

THE PRESIDENT, R. BISHOP CANFIELD, M.D., IN THE CHAIR
REPORTED BY REUBEN PETERSON, M.D., SECRETARY

Reading of Papers

A CRITICAL REVIEW OF FIVE HUNDRED PUBLISHED AND UNPUBLISHED CASES OF ABDOMINAL CESAREAN SECTION FOR ECLAMPSIA.*

REUBEN PETERSON, M.D.

Professor of Obstetrics and Gynecology, University of Michigan.

Three years ago I published the results of an analysis of 530 published and unpublished cases of eclampsia treated by vaginal Cesarean section. Even if the conclusions of that paper have not been accepted in their entirety, at least their presentation has given rise to free discussion and in that way good has resulted. For the past three years I have been engaged in collecting published and unpublished cases of eclampsia treated by abdominal Cesarean section in order that I might be in a position to study carefully the results of this method of treating eclampsia. The work was begun with no idea of proving or disproving the value of this operative procedure in eclampsia. It was proposed to make it a study, an impartial analysis of cases where the uterus had been emptied by the suprapubic route either in the interest of the eclamptic woman or her child. This should be clearly understood at the outset for the value of the work will depend largely upon how the cases have been collected and whether they have been studied with an unbiased mind. Everyone knows how easy it is to prove or disprove anything by statistics, and because this is resorted to so frequently by violent partisans a doubt has arisen as to the value of medical statistics. This is a mistake in my opinion for an impartial scientific statistical study of any medical topic is exceedingly valuable and well-nigh indispensable in judging of the value of certain lines of treatment.

The same method was employed in the collection of the present series of cases as was used in preparing the article on vaginal Cesarean section. Letters were sent to prominent obstetricians, gynecologists and surgeons in this country and abroad stating the purpose of the research work and requesting the privilege of including in the statistics any cases of eclampsia in which abdominal Cesarean section had been performed. In addition the letter stated that the writer would consider it a favor to be referred to any one who had had occasion to treat eclampsia by this method. Through the kindness and courtesy of many correspondents I have been able to gather together for statistical purposes 500 published and unpublished cases of abdominal Cesarean section for eclampsia. When this number was reached the polls were closed, so to speak, in order that the cases could be analyzed and conclusions drawn from such analysis. Otherwise the number could have been indefinitely augmented since at the present time the operation is far more frequently performed than was the case a few years ago.

As in the former paper no case was included in the list where there was not at least one distinct eclamptic seizure. This criterion was established not to emphasize the importance of the eclamptic convulsion but for the purpose of having some standard to go by. For obviously it would have taken us too far afield to include in the list cases where the operation had been performed for the toxemia of pregnancy.

In spite of the fact that more than one-half of the cases, 276 out of 500, were performed by American operators, it is not safe to conclude that relatively abdominal Cesarean section is performed more frequently for eclampsia in this country than abroad since naturally my requests for unpublished cases were complied with more generally in this country. Germany, for instance, furnished over twice as many published cases as did America, ninety-five as against

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forty-six, yet only thirty-three unpublished cases were sent me by German operators.

Of especial interest is the fact that the 500 cases of abdominal Cesarean section for eclampsia represented the work of 259 operators. In other words, the operations were performed not by a few men with large clinical material to draw from and with the skill that comes from opportunities, but by many operators from many countries. This after all is a far better index of the value of an operative procedure for a certain condition than where many operations are confined to a few men whose results perhaps the average surgeon would have difficulty in equalling. For any line of treatment in eclampsia to be of any value must be within the reach of the great body of practitioners, since they see the eclamptic first and must either carry out the treatment or call in someone to do it for them.

The maternal mortality.—Since it is generally agreed that the interests of the mother take precedence over those of her child in a case of eclampsia, it seems fitting that the maternal mortality resulting from the series should be first considered. But I have come to the conclusion that in all fairness to any operative procedure in eclampsia or for that matter any treatment of this complication of pregnancy, the mortality must be arrived at in such a manner as to show its true value. I mean by this that today we are only interested historically in the results obtained by abdominal Cesarean section for any obstetric condition when the operations were performed before the days of asepsis or before obstetricians began to realize the operation under discussion could not be performed safely if prior attempts *had* been made to deliver by the natural passages.

Obstetrics in general and obstetric surgery in particular have been slow to respond to the advances in surgical technic which have taken place during the past thirty years. It is a matter of common knowledge that the operator who is most painstaking in the aseptic technic of his abdominal and plastic work will be guilty of the greatest carelessness in his obstetric surgery. This lack of care is an undesirable inheritance from a host of obstetricians who were not trained in surgical technic, since their surgical experience was limited to this one field. While many deaths resulted from poor technic, so great was the natural resistance of the parturient woman that the mortality from sepsis did not reach alarming proportions so long as the operative procedures were from below, in other words if the peritoneal cavity were not invaded. But it was another story when this happened. Then the mortality was very high for the peritoneum, contaminated by puerperal septic organisms, became rapidly the seat of general inflammation and death resulted from peritonitis.

Since abdominal Cesarean section involves the opening of the peritoneal cavity it is obviously unfair to include in the mortality figures, except for comparison, patients operated by this method before the days of asepsis or before obstetricians realized the contraindications to the operation from the standpoint of sepsis. If such cases are included in the statistics, the figures do not show the results of the treatment of eclampsia by abdominal Cesarean section, but the results of such operative treatment plus sepsis which places the mortality far higher than it should be.

In addition, it must be understood that a small number of cases is of little avail so far as statistics are concerned. Results obtained in the treatment of a few cases may be far different when more patients are subjected to the same treatment. For this reason among others I have waited before publishing results until conclusions could be drawn from hundreds and not dozens of cases.

For the reasons outlined above I have divided the 500 cases chronologically into two groups: first, those occurring prior to 1908 and second, those operated upon between 1908 and 1913. The latter period was selected only because it furnished the requisite number of cases from which to draw conclusions and for no other purpose.

Between 1908 and 1913 there were 283 cases of antepartum eclampsia where the uterus was emptied by abdominal Cesarean section with seventy-three deaths or a maternal mortality of 25.79 per cent. During the first period, that is, up to 1908, there were 198 cases with ninety-five deaths or a mortality of 47.97 per cent. There were twenty-nine cases of the 500 where the year of the operation was not given, therefore so as to be absolutely accurate, these cases were omitted in making up the mortality figures. For the sake of completeness and comparison and for no other reason it may be well to state that in the 500 cases there were 174 deaths or a total mortality of 34.8 per cent.

Inasmuch as the value of the statistics in this paper depends upon the arrangement of the cases in groups from the standpoint of the date at which the operations were performed, further explanation in favor of the plan adopted may be necessary. Total mortalities obtained by collecting cases where operations were performed either before the advent of asepsis or where the latter was imperfectly carried out are of little value for us today. If we wished to obtain an accurate idea of the mortality of the removal of fibroids of the uterus by hysterectomy, either supravaginal or complete, we would not think of collecting operations from the literature appearing during the time gynecologists were try-

ing out different forms of operative technic. Statistics based upon such cases would be quite valueless, so far as our present day viewpoint is concerned. Of what value would be a statistical study of the mortality incident to the operation for appendicitis based upon a series of operations some of them performed in the days when we operated only as a last resort, or waited until an abscess had formed about the appendix?

It is absolutely necessary to study the results of operations by the group methods, if great changes in operative technic have arisen during the period in which the cases in the entire series have occurred. Yet this seems to have been lost sight of in the statistical study of abdominal Cesarean section for eclampsia.

Routh has recognized the necessity of grouping chronologically cases of abdominal Cesarean section performed for different obstetric conditions. He collected 1282 cases of this operation performed by obstetricians and gynecologists of the United Kingdom who were living June 1, 1910. He was able to collect in all 1058 cases of abdominal Cesarean section for contracted pelvis with a mortality of 9.7 per cent. Up to 1891 there were 26 cases with a mortality of 30.7 per cent. while from 1906 to 1910 (uncompleted five years) there were 602 cases with a mortality of 6.1 per cent. Thus if the cases had not been grouped, the mortality for abdominal Cesarean section for contracted pelvis would have stood at 9.7 per cent., while with present day methods it is 3.5 per cent. lower. It also follows the greater the number of cases in the earlier periods, the higher the total resultant mortality will be, hence the greater the error.

So far as I have been able to observe all mortality statistics of abdominal Cesarean section for eclampsia have almost without exception been made without regard to when the operations were performed, hence are valueless so far as furnishing us with a correct valuation of the operation as it stands today. Routh is no exception to the rule, for, while recognizing the necessity for the grouping system as regards his own statistics, he quotes Kettlitz as having collected twenty-eight cases with fourteen deaths, Hillman forty cases with twenty-one deaths, Streckeisen twenty-six cases with eight deaths. The total mortality of the operation in eclampsia in 105 cases was 47.6 per cent. By his own reasoning this mortality must be too high, how much too high could only be ascertained by grouping the cases he quotes.

"Moran collected 116 cases of abdominal Cesarean section from the literature with a maternal mortality of 48.9 per cent. He tries to rectify this unquestionably excessive mortality by grouping 53 cases occurring from 1901 to 1911 with a maternal mortality of 32.32 per cent. But he failed to realize what I have already pointed out that obstetric surgery and especially abdominal Cesarean section have not advanced as rapidly as have other departments of surgery. Only within the past five years has it begun to dawn upon the mind of the obstetric surgeon in general that we can not remove the child by the suprapubic route without a high maternal mortality if attempts have been made to deliver from below or even if many vaginal examinations have been made."

I have been rather insistent upon explaining the necessity of the group method of making up mortality statistics since totally erroneous figures are quoted by those who oppose the operative treatment of antepartum eclampsia. Zinke, for instance, quotes Moran's 32.32 per cent. mortality and says "if this is advancement, the writer fails to see it." The same writer quotes Routh as reporting seven cases of Cesarean section for eclampsia with four deaths or a mortality of 57 per cent. and then adds "Think of it." The great trouble is the lack of thinking going on all the time in regard to mortality statistics. Zinke might just as well have picked out a single case report where death followed the operation and asked us to think of a 100 per cent. mortality. What has the mortality resulting from seven cases to do with any question? When will we learn that statistics made up from less than one hundred cases of any condition must be quoted with reservations?

Dr. Zinke is impressed with the importance of the results of his last thirty cases of eclampsia treated medicinally with a maternal mortality of 13.3 per cent. Such results are to be commended because so many mothers out of the thirty lived but the series is rather small to be of any great importance in determining the value of any kind of treatment. His next thirty cases may show very different results. A small number of cases can be used to prove almost anything. By using this method Zinke's claim to the superiority of medicinal over operative treatment of eclampsia could be overthrown at once by statistics furnished by one operator in my own series. This operator had fourteen abdominal Cesarean sections for eclampsia with one death or a maternal mortality of 7.14 per cent. Still one would hardly claim this to be the average mortality of eclampsia treated by abdominal Cesarean section.

In a previous article certain figures were given of the results of the five operators sending in the largest number of cases (9.5 per cent. mortality in 42 cases) and the mortality of 120 cases furnished by twenty operators having five cases or more. Since these figures were published it has been found that some of these twenty operators had been credited with cases in reality performed by others but reported by them in correspondence. The corrected list shows that during the period from 1908 to 1913

thirteen men performed five or more abdominal Cesarean sections for eclampsia. In all there were 91 cases with seventeen deaths or a maternal mortality of 18.68 per cent. This is a remarkable showing for a series numbering nearly one-fifth of the entire series of five hundred cases.

The mortality records of the different operators vary from no mortality at all up to 60 per cent., always keeping it clearly in mind that the percentages are made up from a small number of cases. I have no means of knowing the conditions of Henkel's and Mullally's patients before operation but Davis has explained the reason for the high mortality in his and Markoe's cases at the New York Lying-in Hospital by saying that their material was made up of many moribund and septic patients. As I shall show later abdominal Cesarean section for eclampsia is contraindicated under these conditions. Deducting the fifteen cases of these two operators we have seventy-six cases with ten deaths or a maternal mortality of 13.15 per cent., by a curious coincidence a fraction of a per cent. less than that quoted by Zinke for his thirty cases treated medicinally.

I am fully aware of the danger of drawing conclusions from such a small number of cases, although the number is over twice as large as that quoted by Zinke. I am also aware that there is danger in excluding cases for apparently good and sufficient reasons, hence I have been careful to explain just how and why such exclusions were made and have refrained from drawing conclusions. Still the series in whole or in part is interesting as showing the results of abdominal Cesarean section for eclampsia in the hands of men who have had experience with the operation under consideration.

While 25.79 per cent. can not be considered a low maternal mortality for the treatment of eclampsia, it is surprisingly low for abdominal Cesarean section in this complication of pregnancy. An operation carrying with it a 40 or 50 per cent. mortality would only be persisted in because of urgent necessity, never as a matter of choice. If, however, the figures stand at 25 per cent. with every prospect of being still further reduced if certain features making for a high mortality can be eliminated, abdominal Cesarean section at least must be given a respectful hearing as a treatment of certain cases of eclampsia provided operative treatment is to be employed.

Later, certain facts will be brought forward explanatory of the high mortality (25.79 per cent.) attendant upon this operation, that is, high as compared with other methods of treatment. Now I merely wish to emphasize the fact that the old mortality figures of this operation for eclampsia are incorrect.

In another article I have proved the advantages of operative delivery in eclampsia over medicinal treatment and spontaneous labor. In 200 cases of eclampsia occurring between 1900 and 1912 where the patients were delivered spontaneously the maternal mortality was 18.96 per cent. while in 1496 cases treated by operative delivery during the same period the maternal mortality was only 14.8 per cent., an advantage of 4 per cent. in favor of operative delivery.

The advice of those who urge the medicinal treatment of eclampsia while the woman is undelivered is irrational as a working rule. Certainly it does not give the operative treatment of eclampsia a fair show, for its advocates say, "use every means except surgical in antepartum eclampsia and then if the fight is going against you empty the uterus." There can be only one result of such delayed operation, a high maternal and fetal mortality.

While the number of antepartum convulsions may not be an exact index of the patient's condition, in a general way they do furnish this information. The chances of an eclamptic with one convulsion are infinitely better than are those of the patient who has had twenty-five. But it is a mistake to endeavor to compile statistics from what follows a certain number of convulsions. Especially is this true if we are dealing with a small number of cases. For instance, it was a mistake in my former article to give the mortality percentages separately after from one to ten convulsions. Immediately the eye took in the fact that the table showed that the maternal mortality where the operations were performed after the first convulsion was 18.51 per cent. while in fourteen cases where the operations were performed after the ninth convulsion the mortality was only 7.14 per cent. Although this was explained in the text, the explanation counted for little.

The convulsions in relation to the maternal mortality have been considered in two large groups, first all the cases between 1908 and 1913 arranged according to whether the operations were performed after from one to five convulsions or after six or more convulsions. The second group has been worked out in a similar manner as regards the time after the convulsions the operations were performed but has also been arranged according to whether the convulsions ceased or continued after the operations.

(a) There were 213 cases in the first group. Of these there were 124 operations after from one to five convulsions with 25 deaths or a maternal mortality of 20.32 per cent. This is an exceedingly low mortality from an operative procedure which has been thought to carry with it a death rate of nearly 50 per cent. It will be noticed that the mortality is 5 per cent. lower when the operations have been performed

after a few convulsions than where there has been delay in emptying the uterus.

If to this immediate emptying of the uterus or at least its emptying shortly after the onset of the convulsions be added non-contamination of the puerperal tract from below by the avoidance of or limitation of vaginal examinations or attempts at delivery a maternal mortality is found which more nearly represents what should be accomplished by the suprapubic route. For out of the 124 operations there were sixty where no or only one or two vaginal examinations were made and where no attempts were made to deliver from below. There were only nine deaths after these sixty operations or a maternal mortality of 15 per cent. Granting this to be a small number of cases, as far as they go they indicate that in clean cases with clean surgery, performed after a few convulsions the maternal mortality compares very favorably with other forms of eclamptic treatment. Also it holds out a hope that under equally favorable circumstances the same or even better results can be obtained in a larger number of cases.

I have no argument with those who attempt to explain such figures by saying that a large proportion of such operations were probably useless and that many of the patients would have recovered without them. Such statements are as worthy of notice as would be the suggestion that probably the drugs used in the medicinal treatment of eclampsia were inert and therefore might just as well not have been administered. The point is that the patients were eclamptics as shown by the convulsions and other symptoms and that they recovered after the uterus was emptied by the suprapubic route. This does not mean that every woman with eclampsia should be subjected to the same treatment or that equally good results may not be obtained by other methods. That is another question altogether and must be considered separately. But nothing is gained by trying to explain a mortality by suggestions which do not explain and besides are foolish in the extreme.

The increase in mortality due to delay is shown by the fact that in eighty-nine eclamptics where the operations were performed after the sixth convulsion there were twenty-seven deaths or a mortality of 30.33 per cent. This is 10 per cent. higher than after quick delivery and 5 per cent. higher than the total mortality during this same period.

(b) Where there is a cessation of convulsions after the uterus has been emptied the presumption is that the patient is in better condition than where the convulsions continue, although, as we have seen, death occurs in a certain percentage of these cases. But these deaths may have occurred from delay in operating even if no convulsions follow. This is shown by the fact that in sixty cases where there was a cessation of the convulsions after the operations where the latter were performed after from one to five convuulsions, there were eight deaths or a maternal mortality of 13.33 per cent. In fifty-two cases under the same conditions except that the convulsions continued there were fourteen deaths or a mortality of 26.92 per cent. We are forced to the conclusion then that this double as high mortality was due to the fact that even with immediate operation after the onset of the convulsions the patients were so toxemic that death followed in spite of operative treatment.

Where the abdominal Cesarean sections were performed after more than five convulsions in thirty-eight cases there were ten deaths or a mortality of 26.31 per cent. where there were no convulsions after the operations. In forty-four cases under the same condition, except that the convulsions continued, there were sixteen deaths or a mortality of 36.36 per cent.

From 1908 to 1913 there were 248 children delivered by abdominal Cesarean section with nine deaths or a fetal mortality of 3.62 per cent. Up to 1908 there were 133 cases with sixteen deaths or a fetal mortality of 12.03 per cent. Thus it will be seen that the fetal mortality in the first period was almost four times as great as that during the five year period, from 1908 to 1913.

Just as the maternal mortality was lowest when the uterus was emptied early after the first convulsion, so the lowest fetal mortality (2.54 per cent.) occurred in the period from 1908-1913 where the operations were performed after from one to five convulsions, that is, under good technic and that before the child as well as the mother was overwhelmed by the eclamptic toxin. Faulty technic probably accounted for double this mortality up to 1908 for in both groups of cases the operations were performed equally early.

The highest fetal mortality (26.52 per cent.) was found in forty cases where the operations were performed before 1908 and after six or more convulsions. Even in the five year period the fetal mortality is high (7.89 per cent.) compared with the 2.54 per cent. mortality obtained through prompt operating and good technic.

Zinke in thirty cases of eclampsia reports a fetal mortality of 50 per cent. Lichtenstein after certain exclusions had a fetal mortality of 25 per cent. in fifty children born after the venesection and narcotic treatment. After various methods of delivery with some exclusions in 1487 cases there were 460 children died or a fetal mortality of 31.2 per cent. In the light of such figures the obstetrician is bound to consider the rights of the fetus when by a certain operation the fetal mortality can be

reduced to 2.54 per cent. with a maternal mortality in sixty cases of 15 per cent.

Vaginal examinations prior to the abdominal Cesarean sections and the maternal mortality.—It is exceedingly difficult to obtain from published cases or from the questionaire accurate information regarding possible contamination of the genital tract through vaginal examinations. Routh's analysis of abdominal Cesarean section cases has shown the danger of frequent examinations or attempts at delivery since the maternal mortality under these conditions is 34.3 per cent. in comparison with 2.9 per cent. where the operations have been performed when the patients were not in labor and the membranes unruptured. But it is too much to expect that any great proportion of eclamptics will be subjected to abdominal Cesarean section without first being subjected to thorough examination, nor could this be desirable. In the great majority of cases eclampsia comes suddenly without warning and without previous knowledge of the size of the bony pelvis or the soft parts. Hence at least one vaginal examination is almost always necessary.

Again, it is impossible to ascertain from a questionaire the manner in which the vaginal examinations were made. It is perfectly possible to make a number of such examinations in accordance with an aseptic technic so perfect as to be almost without danger. On the other hand it is equally possible to infect the woman through a careless technic by one vaginal exploration.

In 188 cases during the five year period it was distinctly recorded that one or more vaginal examinations were made. There were fifty-five deaths among these patients or a maternal mortality of 29.25 per cent., distinctly higher than the total maternal mortality (25.79 per cent.) during this period. Again combining the few cases where it was distinctly stated that no vaginal examinations were made with those cases where no statement was made, ninety-five in all, we find there were eighteen deaths or a maternal mortality of 18.94 per cent.

As far as this evidence goes we are justified then in concluding that a certain proportion of the deaths during the five year period were due to prolonged or badly conducted vaginal examinations with the understanding that such examinations would have been productive of far less mortality had not the peritoneal cavity and the uterus been opened subsequently.

Summary and Conclusions.

1. Since the 500 cases of abdominal Cesarean section represent the work of 259 operators they are a very fair index of the present status of the operation as a method of treating antepartum eclampsia.

2. Since the results of operative obstetrics, especially abdominal Cesarean section are far better at the present time than formerly, the value of the operation as a method of treatment of eclampsia can only be judged by grouping the cases chronologically.

3. Between 1908 and 1913 there were 283 cases of eclampsia treated by abdominal Cesarean section with seventy-three deaths or a maternal mortality of 25.79 per cent. Up to 1908 there were 198 cases with ninety-five deaths or a mortality of 47.97 per cent. Hence the maternal mortality in the five year period has been reduced nearly one-half.

4. Hence the old figures of a 40 to 50 per cent. maternal mortality from abdominal Cesarean section for eclampsia are incorrect and should no longer be quoted.

5. The mortality percentage quoted above (25.79) probably can be considerably lowered by care in technic and by not making use of the suprapubic route where there is great probability that the woman has been infected from below.

6. Nearly one-fifth of the entire series, ninety-one operations, were performed by thirteen men having five or more cases to their credit, with seventeen deaths or a maternal mortality of 18.68 per cent.

7. Deducting fifteen cases where the proportion of moribund and septic patients was very high, the remaining seventy-six cases with ten deaths give a maternal mortality of 13.15 per cent.

8. Although an eclamptic may die after a single or survive after many convulsions, the latter must be utilized as an indication of the degree of eclamptic poisoning until we have a better method of estimating the patient's condition.

9. Emptying of the uterus either spontaneously or by artificial means while it puts a stop to the further elaboration of toxins from the fetus, the placenta or both, may not be sufficient to prevent further convulsions or in certain cases death of the mother from intoxication. In other words, so great has been the effect of the poison that convulsions continue after delivery or death ensues in spite of the relief afforded by emptying the uterus.

10. In the present series convulsions ceased after abdominal Cesarean section in 251 out of 457 cases or in 54.92 per cent. These statistics agree with those made up from thousands of cases of eclampsia showing that convulsions cease after the emptying of the uterus either spontaneously or artificially in from 52 to 62 per cent. of the cases.

11. Even where the convulsions cease after delivery a certain proportion of the patients die. In 146 cases where the convulsions ceased after abdominal Cesarean section during the five

year period (1908-1913) there were 41 deaths or a maternal mortality of 19.8 per cent.

12. While the above percentage of patients died after emptying the uterus by abdominal Cesarean section after cessation of the convulsions the mortality is much less than where the convulsions continue, since in 130 of such cases there were forty-one deaths or a maternal mortality of 31.53 per cent.

13. The operative treatment of eclampsia has never been given a fair trial. To do this the uterus should be emptied quickly, as soon as possible after the onset of the first convulsion, not emptied after all kinds of medicinal treatment have been tried and failed.

14. In the present series there were twenty-five deaths after 124 operations performed after one to five convulsions or a maternal mortality of 20.32 per cent.

15. The best results in the operative treatment of eclampsia are bound to follow immediate emptying of the uterus in cases where the woman has not been infected by frequent vaginal examinations or attempts at delivery from below. This is shown by the following:

16. In sixty of the 124 cases where the operations were performed after from one to five convulsions, where no or only one or two vaginal examinations had been made and where no attempts were made to deliver from below there were only nine deaths or a maternal mortality of 15 per cent.

17. The increase in mortality due to delay is shown by a mortality of 30.33 per cent. where the operations were performed after the sixth convulsion. This is 10 per cent. higher than after quick delivery and 5 per cent higher than the total mortality resulting during this same period (1908-1913).

18. In sixty cases where the convulsions ceased after operations performed after from one to five convulsions there were eight deaths or a maternal mortality of 13.33 per cent. The mortality is twice as high (26.92 per cent.) after operations performed under the same conditions except that the convulsions continued.

19. Where the abdominal Cesarean sections were performed after more than five convulsions there was a resulting mortality of 26.31 per cent., where there was cessation of the convulsions, and 36.36 per cent. where they continued.

20. The average number of convulsions in 386 cases of eclampsia in the abdominal Cesarean series was nine where the cases were not grouped. The average was ten up to 1908 and eight from 1908-1913.

21. Twins occurred twenty-one times in 500 cases of abdominal Cesarean for eclampsia or in 4.02 per cent. of the cases. This is over three times as frequent as are twins in normal cases.

22. Excluding premature children and counting all children as living who survived one hour after delivery there were nine deaths from 1908-1913 where 248 children were delivered by abdominal Cesarean section or a fetal mortality of 3.62 per cent. Under the same conditions the fetal mortality was 10.69 per cent., if children dying the first three days after delivery were counted among the deaths. Even estimating the fetal mortality by this method it is much better than by any other method of treating eclampsia.

23. The fetus as well as the mother is affected by the eclamptic poison. The greater the number of eclamptic convulsions before delivery the greater the fetal mortality. Hence for the sake of the fetus the uterus should be emptied as soon as possible after the first convulsion. If other factors in the case call for abdominal Cesarean section the chances of the fetus will be much better than if another method be employed.

24. In 474 cases of eclampsia in the present series, 83.75 per cent. were primiparae and 16.17 per cent. multiparae. The relatively larger proportion of primiparae was due to the fact that primiparous conditions, such as undilated and rigid cervix and rigidity of the soft parts more often called for the abdominal operation than for other methods of delivery.

25. The maternal mortality is higher after abdominal Cesarean section in multiparous women than is the case with primiparous eclamptics. In the present series in 225 primiparae the maternal mortality was 24.44 per cent. while in forty-eight mutiparae the mortality was 27.08 per cent.

26. The fetal as well as the maternal mortality is higher in multiparae after abdominal Cesarean section. This is probably due to the greater degree of intoxication among the multiparae since, in both primiparae and multiparae, the children, because of the nature of the operation employed, escape the traumatisms of labor. The greater intoxication among the multiparae is probably due to their being on the average older than the primiparae, the average age of the former in seventy-seven cases being 32.6 years while the average age of the latter in 397 cases was 24.6 years.

27. The maternal mortality in eclampsia after abdominal Cesarean section steadily increases with the age of the patients, it being 23.63 per cent. between the ages of sixteen and twenty and 31.11 per cent. between the ages of thirty-one and thirty-five.

28. The number of eclamptic cases in the present series steadily increased from the fifth month of gestation up to full term, also the further advanced the pregnancy, the lower the maternal mortality.

29. Unless the aseptic technic employed in attempts to deliver from below be known, ab-

dominal Cesarean secion is contraindicated, so great are the dangers of fatal peritonitis when the patient is infected.

30. The high death rate of abdominal Cesarean section after operative procedures is shown by the fact that there were ten deaths in twenty-nine such cases or a maternal mortality of 34.48 per cent. This 9 per cent. increase in mortality over the total mortality (25.79 per cent.) during the same period was undoubtedly due to sepsis, shock and delay in emptying the uterus.

31. The mortality is distinctly higher after abdominal Cesarean section in eclampsia, if vaginal examinations have been made prior to the operations. The danger increases directly with the number of examinations made and the lack of asepsis employed.

32. Any obstetric condition which makes delivery by the natural passages prolonged and difficult may be an indication for abdominal Cesarean section in eclampsia. If delivery be decided upon the uterus should be emptied by the method which will perform the work the quickest and with the least trauma and shock to mother and child. However, it must be borne in mind that there is more danger of sepsis when the peritoneal cavity is opened.

33. With the present state of our knowledge of this operation for eclampsia it can not be denied that older and more tried methods of emptying the uterus in eclampsia give better results in eclamptics with normal pelves and soft parts, hence should not be lightly discarded in favor of the more brilliant and more easily performed abdominal operation.

34. But with a maternal mortality after abdominal Cesarean section of 18.68 per cent. in 191 cases of eclampsia in one series, 13.13 per cent. in seventy-six cases in another and 15 per cent. in sixty cases where the uterus was emptied after a few convulsions, the operation under consideration has reached a stage where it can no longer be disregarded by obstetricians who have based their opposition to the procedure upon statistics which were altogether too high.

DISCUSSION.

Dr. Harry B. Schmidt: I would like to ask Dr. Peterson if he has ever tried to estimate the amount of nitrogen retention in these cases as a test of the severity of the eclampsia.

Dr. Frederic M. Loomis: I think one of the striking lessons of this paper is that we must insist that our students do not make reckless vaginal examinations of women who are about to go into labor. I was recently told by a student from another school with a large out-patient service that it is the custom there to send two or three to a case, each one making a vaginal examination, usually without gloves. This is absolutely inexcusable. A very satisfactory examination can be made by rectum without any danger of infecting the woman, and while eclampsia is not common, I think we should place its spectre beside that of sepsis, and so conduct every labor and every examination that we can safely open the abdomen if necessary later.

Dr. Conrad Georg, Sr: I should like to ask about how many cases Dr. Peterson has seen of eclampsia after the uterus has been emptied. I want to know what mortality he has seen in this variety of eclampsia.

Dr. Reuben Peterson: I would say in reply to Dr. Schmidt's question that up to the present time I don't think any satisfactory method has been worked out to determine the exact condition of the eclamptic. Of course there have been various attempts to do so but as far as I can see, these tests haven't been very satisfactory and we aren't very much better off today than formerly. I don't think that the test you speak of has been used very extensively. In answer to Dr. Georg's question, I may say that I have seen quite a good many cases of postpartum eclampsia. The mortality in these cases is from 10 to 15 per cent. At first sight it would seem as if that would speak against the treatment of emptying the uterus in antepartum eclampsia. The uterus is emptied and after some hours or even days the woman is taken with eclamptic convulsions. That would seem to be against the argument that the uterus should be emptied as a treatment of eclampsia, but in reality it is not. The eclamptic has convulsions prior to and after the emptying of the uterus because of the amount of intoxication present. I have had a number of such cases. One of these was that of a woman in which I had no idea that the patient was in a dangerous condition. Two hours after I left the house she was seized with a violent eclamptic convulsion in spite of the fact that the uterus had been emptied. In these cases the damage has already been done, the damage to the higher nerve centers, liver, kidneys or brain and in spite of the benefit of the emptying of the uterus. It is just the same in surgery. You have a patient with appendicitis who dies following operation. The surgeon is careful to explain that the patient died, not from but in spite of the operation—in spite of the benefit derived from the surgical procedure. So in spite of the fact that you empty the uterus, the woman is so intoxicated by prior conditions that she continues to have eclamptic seizures. She has been so overwhelmed by the toxins that in spite of the relief resulting from emptying the uterus, postpartum convulsions occur.

SUMMARY OF RESULTS FROM 600 INTRAVENOUS INJECTIONS OF NEOSALVARSAN.

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As the sum total of knowledge concerning salvarsan and neosalvarsan has increased, the methods of their administration have changed. In the last twenty months, approximately 1239 injections have been given in the Dermatologic clinic with no fatalities and only a very few untoward results. Since the last of September, 1913, 600 injections in 160 cases have been administered. At that time the concentrated method of Ravaut was introduced by Dr. Wile and has been used since to the exclusion of other procedures. By this method a hyper- or iso-tonic solution of neosalvarsan in freshly dis-

tilled sterilized water is made and immediately injected. Under aseptic precautions the contents of a nine decigram ampoule are dissolved in ten cubic centimeters of water. This is aspirated through a cotton filter into an all glass Luer syringe. A needle is substituted for the filter and the required dose immediately injected into a vein of the arm in the usual manner. This method was first introduced by Dr. Paul Ravaut of the St. Louis Hospital in Paris. It possesses decided advantages over the previous procedure in which from 120 to 300 cubic centimeters of water or salt solution were used as a solvent. By using ten cubic centimeters of freshly distilled sterilized water as a solvent, several uncertain and unreliable factors in the production of salvarsan reaction were eliminated. Wechselman demonstrated several months ago that water, although sterilized, will produce severe reactions if allowed to stand too long previous to injection. This was thought to be caused by spores or from endotoxins from killed organisms, other observers accusing chemical impurities such as salts of lead silicates, calcium carbonate and finally the sodium chloride used to make the solution iso-tonic. As a result, distilled water was used, but this was strongly hemolytic and probably determined many of the untoward phenomena occurring after repeated injections. Ehrlich also showed the increasing toxicity of the drug resulting from oxidation upon prolonged manipulations preceding injection. These objections were practically all removed by the concentrated dose method. The whole procedure need not occupy more than three to four minutes from the opening of the ampoule to the withdrawal of the needle from the vein.

In this clinic the number of injections and dosage of each has been largely determined by careful study of the individual patient; since a large number of our patients are in the secondary period and because it is advisable to state a definite time for residence in the Hospital, approximately the following plan has been followed. Four injections are usually given, the second one occurring two days after the first and the other two at five day intervals. The successive increase in dosage is as follows; for an average man .4, .6, .8, and .9 Gr. for the last. For the average woman doses of .3, .5, .7 and .8 Gr. are used. This dosage varies considerably according to the physical condition of the patient. A hospital residence of about three weeks is required for this course of treatment. In children suffering from hereditary lues the method and dosage was varied, only one injection per week being given. In a number of cases, more than four injections were given, one patient with a rupial syphilid receiving ten injections without reaction.

In practically all cases the therapeutic results were excellent and coincide with the results of other observers. Mucous membrane lesions healed most rapidly, and secondary lesions were in almost all cases entirely involuted at the time of discharge. The most resistant lesions from a dermatologic standpoint were some of the gummata.

Practically all patients showed an increase in hemoglobin, in weight and in general health and in most cases a feeling of wellbeing succeeded the first injection. Moderately advanced secondary syphilitic anemias cleared up rapidly. Those of the primary type and some of more doubtful diagnosis did not do so well. However, even in this class, with one exception there was marked improvement following the injections.

Several cases of nephritis were treated with no untoward results, although one cannot say in view of the recent findings of Wechselman that the treatment is not without considerable danger. One patient with a blood pressure of 212 received four injections of .2, .25, .45 and .3 Gr. with no noticeable reaction. Another patient showing advanced chronic interstitial nephritis and diabetes received two injections of .3 to .5 Gr. with no bad results.

One patient, six months pregnant, with profuse secondary lesions of the mouth and skin received four injections of .4, .6, .8, and .8 Gr. followed by mercurial treatment. As a result, she was delivered of a full term apparently healthy child who, however, showed suggestive stigmata and about thirty days later a bullous eruption on the feet and arms. This result does not corroborate the sanguine report of Jeanselme who reported healthy children after similar treatment.

A case of obstructive syphilitic laryngitis showed a rise in temperature of 100.4 degrees after his first injection of .3 Gr. and some fourteen hours later an increase in the laryngeal obstruction with great difficulty in breathing. Succeeding injections of larger amounts did not cause any reaction. This is an illustration of the so-called Herxheimer reaction.

Another rather striking reaction occurred in a patient who had an intravenous injection of salvarsan three months preceding his entrance into the Hospital. Within five days after reserving .3 Gr. of neosalvarsan he developed a seventh nerve palsy of the left side. This entirely cleared up after the subsequent injections. Inflammation of the optic, auditory and facial nerves occurred in a small number of cases after salvarsan. They also occur with no treatment and after treatment with mercury.

A case of advanced secondary optic atrophy in the tertiary period became much worse after two small injections. The patient was an advanced tabetic. A number of cases have shown marked slowing of the pulse succeeding the first

injection. In a case of late secondary lues, a patient addicted to the excessive use of tobacco showed a marked slowing of the pulse and a subnormal temperature. The slow pulse persisted for some days. Succeeding injections were well tolerated.

Another case developed a temporary slowing of the pulse and a subnormal temperature about seven hours after his seventh injection. This was associated with dizziness and stupor. The symptoms subsided after stimulating measures. No further injections were given in this case.

Classifying the more common reactions, it was found that there were twenty-four after the first injection; ten after the second; ten after the third and seven after the fourth. Of the twenty-four following the first injection nine were Herxheimer reactions which consist in the temporary exacerbation of previous lesions and symptoms. This reaction is explained either because of the liberation of endotoxins from the destroyed spirochete or by a stimulation of the spirochetes by a dose of the drug insufficient to cause their death. Six patients showed a rise in temperature above 100 degrees. Four were nauseated. Two showed a decided fall in pulse and temperature and two suffered from severe headache associated with nausea. Persistent heachache in the secondary period has usually indicated cerebrospinal involvement. One patient exhibited a transient hematuria which did not occur after succeeding injections.

After the second injection there were ten reactions. Four of these showed an erythematous eruption which was taken as indicating their limit of tolerance. Three patients reacted with a temperature of from 101 to 103 degrees. Two suffered from headache and fever and one from nausea. It is apparent therefore, that after the second injection the most probable cause of reaction is that of drug intolerance.

There were ten reactions after the third and seven after the fourth injection, most of which, were examples of intolerance to the drug, as indicated by an erythematous eruption frequently associated with a febrile disturbance. After such manifestations salvarsan medication was discontinued and treatment was continued with mercury. There were two reactions with a subnormal pulse and temperature, one after the third and one after the fourth injection. The exact cause of this reaction cannot be given but it is held that in part, at least, they are due to the effect of the drug on the vagus. Two patients who had some six or eight injections complained of a tingling in the hands and feet. This gradually disappeared upon cessation of treatment.

Credit is due to Professor Wile for the inception and supervision of the mode of treatment as outlined in this paper.

Judging from the result of these six hundred injections, it seems justifiable to draw the following conclusions.

1. The intravenous administration of neosalvarsan in selected cases is without danger.
2. Danger is minimized by the method making sure of a concentrated hypertonic solution.
3. Danger is minimized by keeping the patient under hospital supervision while undergoing treatment.
4. In the absence of a large number of spirochetes, a certain amount of reaction is inevitable after the first injection. This reaction is of no importance.
5. A reaction of sensitization is excited in a small number of cases.
6. The small number of untoward results is due to care in selecting cases, proper dosage and asepsis in administration.
7. While neosalvarsan has not proved as potent as old salvarsan, it is highly efficient and may be used more often and in larger doses.

DISCUSSION.

Dr. Udo J. Wile: I think the most important lesson we have learned from the 600 or so cases treated by the concentrated method and the 800 or 900 treated by the dilute form, is not when to give salvarsan but when not to give it. There are certain definite contraindications that the reactions have shown. Defective elimination of any sort whatever constitutes a very definite contradindication. We have been very careful in these cases to give neosalvarsan only upon the responsibility of the department which transferred the case to us or to substitute mercurial treatment in these cases. The reason for this is that arsenic is not toxic for the individual whose elimination is physiologically correct. As soon as this substance is stored up in the body for any time it breaks down into metallic arsenic, the degree depending upon the slowness of the elimination of the drug.

As to the relative value of the concentrated over the dilute method of administering neosalvarsan, there can be no shadow of a doubt. A large amount of fluid---20 cubic centimeters of water for each decigram, making 120 for the maximum ampoule, invariably causes a certain amount of hemolysis and more or less anemia after repeated injections. Ravaut showed definitely that when the blood is allowed to flow back into the syringe, it can be kept in this solution for an indefinite time without laking. And again, the blood pressure is not appreciably raised by the increase of 10 cubic centimeters of fluid. But it is raised by a larger quantity. Such a rise of blood pressure is not dangerous to the average patient, but to a patient who is already a high pressure case, this increase is of great moment.

There can be no doubt in anybody's mind that the old salvarsan is much more potent than neosalvarsan We still use the neosalvarsan because the patients are usually unable to stay in the Hospital long enough to receive the old in repeated doses. We give an average of five injections of the neosalvarsan. In my own experience I have given twenty-two injections to one patient and as high as two grams of neosalvarsan or 1.5 of old salvarsan as a terminal dose. The initial dose should invariably be small in order to test out the patient's possible idiosyncracy. The technic which has been followed in this clinic is such as one should observe in

a capital operation—absolute asepsis and careful record of cases.

DR. WILLIAM D. LYON: In Edinburgh I saw Dr. Findlay treat many out-patient infants by this method of neosalvarsan. He was not particularly careful as to technic. Most children were kept a half hour or longer after the injection. He gave a large dose to each infant. The results so far as symptoms were concerned were exceedingly good. As to the effect on the lesions, the results were very good. Some infants seemingly in very bad condition, became very comfortable in just a few days after the first or second injection. The lesions melted away like snow.

DR. CONRAD GEORG, SR.: Has Noguchi's discovery of the spirochetes in paralysis made any change in the treatment or in mortality? And in cerebellar lues are these salvarsan treatments of any special benefit over the treatment by mercury, sufficiently guarded? And another question I want to ask. Is cerebellar ataxia without any symptoms that indicate tabes to be looked upon as cerebellar lues or progressive paralysis? In a case where there is no disturbance of sensation, peripheral or deep, no eye symptoms you can refer to tabes—nothing pointing to cerebellar ataxia?

DR. ALVIN J. LORIE: I would like to ask why records of the use of neosalvarsan show it to be more efficacious in secondary than in primary lues so far as a negative Wassermann reaction is concerned.

DR. JOHN T. HOLMES: In answer to Dr. Georg's first question I would say that in cerebrospinal lues the treatment by the intravenous injection of any drug is rather unsatisfactory. Dr. Camp determined sometime ago that none of the salvarsan was found in the spinal fluid after intravenous injections of salvarsan. Personally, it seems to me that there is not much to offer in cerebrospinal lues through salvarsan. any more than in mercury properly given. Of course, the new method of treatment by salvarsanized serum and by other intradural medicaments, offers the greatest hope for this class of nervous involvement. The reports are exceedingly good it seems to me, when we consider the hopelessness of such cases previously. In reply to Dr. Georg's other question, I think it is a question of diagnosis rather than treatment. A case of that sort I should certainly refer to a neurologist. In regard to Dr. Lorie's question, I would say that I did not know that that was true. Perhaps Dr. Wile can inform you about the matter.

DR. R. BISHOP CANFIELD: I would suggest that such a patient had meningo-encephalitis, one of the most important changes that take place in the brain in syphilis. Salvarsanized serum would probably be the best thing for him.

DR. UDO J. WILE: I would say that it didn't belong to the tabetic class of patients nor to progressive paralysis. I would like to differ with Dr. Holmes that the treatment of cerebrospinal syphilis lies in the introduction of salvarsanized serum into the cerebrospinal canal. Spinal cases, including the brain in cases of cerebrospinal syphilis hold out hope for amelioration only in so far as the active spirochetes can be killed off. They can be much better killed off by dilute injections of neosalvarsan intradurally than by salvarsanized serum. I should say that the future treatment of cerebrospinal syphilis lies in the introduction of a drug allied to salvarsan, which shall be parasitropic and at the same time not neurotropic. The present objection to salvarsan used intradurally is that it is actively neurotropic.

DR. CONRAD GEORG, JR.: I should like to ask about the patients in Los Angeles who died from the effects of salvarsan injections.

DR. UDO J. WILE: That was due to the fact that the drug had been allowed to stand. The patients died from acute encephalitis. Progress is being made in the treatment of progressive paralysis. An attempt is being made to treat these patients intradurally. We have started treatment of cerebrospinal syphilis by intradural injections of very dilute neosalvarsan. I have just reported a series of twenty-five injections in fifteen cases in some of which we have had gratifying results and in some not so gratifying.

A CASE OF OTITIC STREPTOCOCCIC BACTEREMIA.

R. BISHOP CANFIELD, M.D.

(From the Clinic of Otolaryngology, University Hospital, Ann Arbor, Michigan).

I wish to put on record the following case of otitic streptococcic bacteremia: The patient is Marjorie J. aged 9 years, who entered the University Hospital May 4th, 1914, with the following history: Two weeks ago she contracted measles. A few days later it was noticed that the right ear was discharging although the child had not complained of pain in that ear. The discharge was at first a bloody serum but soon became purulent and has persisted until the present time. Three days after the discharge appeared the child had a severe chill lasting about ten minutes. About this time her temperature was found to be 105 degrees Since the first chill four others have followed but none has been so severe as the first one. She has complained of frontal headache and has vomited several times.

Examination.—The child is lying on her left side in the active position. The thighs are flexed somewhat upon the abdomen and the legs are flexed upon the thighs. The left arm is held quietly but the right arm is moved freely. The face is pale and the expression is anxious. She replies to questions intelligently but is irritable and peevish. The chest and abdomen are negative. There is moderate desquamation on the flexor surfaces. There is no König or Babinski and the deep reflexes are prompt and equal. The left elbow is warmer than the right but swelling is not noted. She complains bitterly upon movement of the left elbow. The eyes are negative. The left ear is negative. The right ear shows the tympanic membrane red and bulging. There is a perforation in the posterior half through which pus appears. The posterosuperior canal wall droops in the depths of the canal. The mastoid is tender over the tip and the posterior surface of the bone. The blood showed reds 4,720,000, whites 9,900 with 74 per cent. polys.

A diagnosis of acute mastoiditis with sep-

ticemia was made and in view of the character of the discharge from the ear and of the clinical course as learned from the history the infecting organism was thought to be streptococcus pyogenes.

May 5th a complete mastoid operation was performed. The mastoid process was found to be diploetic in character and was filled with pus and plastic lymph. The character of the mastoid and the appearance of the sigmoid sinus when uncovered substantiated our opinion that this was a case of sepsis without thrombosis. The sinus was opened and this condition found to exist.

On the day following the operation, the blood culture which had been taken on the day before the operation showed a distinct growth of streptococcus pyogenes. There was no improvement in the patient's general condition. She was colorless, listless and apparently oblivious to her surroundings. The temperature rose to 104 deg. at 8 p. m. and the body became covered by a dull red rash suggestive of sepsis. Thirty cubic centimeters of human blood serum were given subcutaneously. From then on blood serum was administered intravenously, the attempt being made to give at least fifty cubic centimeters. Through errors in technic a part of this was lost on more than one occasion. Following each transfusion there seemed to be some improvement in the general condition. The temperature on the other hand retained its septicopyemic type. It is interesting to note that the leucocytes which numbered 9,900 on the day of entrance rose after the operation to 14,000-18,000 and remained up. It was apparent that the source of infection of the blood stream had not been satisfactorily dealt with, although daily inspection of the sinus showed nothing pathologic. On the eighth day after the operation, however, a drop of pus was seen coming up from the neighborhood of the jugular bulb. On this account the jugular vein was resected, the lower end of the upper portion being sutured to the skin. A blood culture was taken from the portion excised (later shown to be negative). From this point the child began an uneventful recovery.

This case is put on record as one in which a streptococcic bacteremia was clearly demonstrated and in which the intravenous injection of human blood serum was employed with apparently some improvement in the patient's general condition. This improvement was no doubt an incident in the course of her disease rather than a direct result of the use of the serum.

DISCUSSION.

Dr. Udo J. Wile: I should like to ask whether in the absence of signs or symptoms pointing to endocarditis, there might not still be a valvular condition present?

Dr. Harry B. Schmidt: I took the first blood cultures on this little girl, and both tubes were positive in forty-eight hours showing a long-chained streptococcus. Two days later I took a culture which proved negative. After the second operation a culture from the jugular bulb was negative. She had symptoms which were typical of septicemic foci in the joints, i. e., they were nonsuppurative. I examined this patient's heart a few minutes ago. There is a rapid pulse rate which might be due to septicemia but in my opinion is due to excitement. Otherwise the heart is absolutely negative. I remember when first seeing this patient, I gave her a bad prognosis. I can see that in this case the organism was probably in the jugular bulb and may have entered the blood stream as it does in endocarditis. The organisms are localized on the heart valve, and they enter the blood stream in bunches. When the patient's temperature is normal, one usually finds the blood cultures negative, but during a rise of temperature you will find that the cultures are usually positive.

Dr. Udo J. Wile: Does Dr. Schmidt think that in the absence of all clinical signs one could rule out an endocarditis in this case?

Dr. Harry B. Schmidt: No you can't. The lesions are intramural; they are either underneath the valves or on the chordae tendinae, frequently on the auricular valves.

Dr. Udo J. Wile: I should like to call attention to the high pulse rate that accompanies the onset of this febrile period; this following a period of normal pulse rate and temperature, suggests I think somewhat the onset of an endocarditis.

Dr. Alvin J. Lorie: I have been taking care of this little girl. The neck and mastoid wounds contain a considerable quantity of sloughing material. I have been curetting and painting these wounds with iodine. The patient is extremely nervous. After the dressing, I find that the pulse rate and the temperature rise but drop after she has quieted down.

Dr. R. Bishop Canfield (closing the discussion): I think it is very easy to explain why a patient infected with streptococcic septicemia gets well after the proper surgical measures have been taken. If a thrombosis develops, the sinus becomes full of purulent material. When this clot begins to disintegrate, the patient develops a rise of temperature and chill, and positive blood cultures can be made. If below this thrombus the vein is ligated, the superior sigmoid and petrosal sinuses ablated or removed, you have removed the source of infection from the blood stream. that is, you have removed that portion of the circulatory apparatus infected with the ex-

ception of the portion of the jugular vein extending from the bulb to the point of ligation. If we sew this end of the jugular vein to the skin with catgut, leaving the end open for irrigation of the remaining infected portion, we have removed absolutely the source of infection. All the patient has to do is to overcome the infection remaining in the blood stream. When the original source of the disease has been removed, the patient usually gets well.

In regard to this temperature being characteristic of endocarditis, I think it is characteristic of the streptococcus pyogenes infection; whether the infection is on the heart valve or in the ear makes no difference. A temperature like that is almost pathognomic of the above mentioned infection. If the patient develops a running ear with mastoid disease and throughout the entire course of the disease has no temperature, we are almost certain that it is streptococcus mucosus infection. This is quite characteristic of the streptococcus mucosus whether it is in the heart valve or in the ear.

In regard to Dr. Schmidt's statement about non-suppurative foci being characteristic, in my experience they are no more so than are the suppurative ones, because I have seen plenty of them where abscesses would form in the various parts of the body. Some of these cases at autopsy show multiple abscesses in the spleen, liver and other portions of the body. As a matter of fact, however, these cases in which metastases develop have a rather favorable prognosis because they show some tendency toward localization. If the metastases are in the lung, they don't do much damage. In the heart or brain, of course they are more serious.

TRANSACTIONS
OF THE
CLINICAL SOCIETY
OF THE
UNIVERSITY OF MICHIGAN

STATED MEETING, JULY 27, 1914

THE PRESIDENT, R. BISHOP CANFIELD, M.D., IN THE CHAIR
REPORTED BY REUBEN PETERSON, M.D., SECRETARY

Reading of Papers

CASE OF TABES DORSALIS WITH A MARKED FAMILY HISTORY OF THE DISEASE. OBSERVATIONS ON THE ETIOLOGY OF TABES AND TREATMENT OF THE ATAXIA.

CARL D. CAMP, M.D.

(From the Clinic for Diseases of the Nervous System, University of Michigan.)

Tabes dorsalis, or, as it is often called, locomotor ataxia, is one of the commonest forms of disease of the nervous system. This patient shows certain instructive points which I think may be of interest.

The first point to which I would draw attention is the family history of the patient. His father died, at sixty-three, of uremic poisoning, but having had the symptoms of locomotor ataxia. Two of the patient's paternal uncles had locomotor ataxia. The patient's mother died of pneumonia, with no symptoms of ataxia. One brother has locomotor ataxia and is now under treatment (Swift-Ellis treatment) in a nearby town. Another brother died of paresis. A sister of the patient has tabetic symptoms. Two other sisters of the patient had goiter. The maternal grandparents died of old age and rheumatism. Six members of this family, in three generations, had locomotor ataxia and one other had paresis. As you know, this disease is at present considered to be due to an infection with syphilis. It seems probable, however, that there is at least one other factor to cause the development of tabes or paresis. What this other factor is we do not know, various theories having been advanced. The most popular theory at the present time is that there are different strains of spirochete, and that some of these strains especially affect the nervous system. In the case presented this evening it would seem improbable that three generations of the same family could derive a syphilitic infection from the same source. In fact, it also seems improbable that the same strain of spirochete should be present through three generations unless the disease was inherited. The patient shows no signs of inherited syphilis, such as Hutchinson teeth, etc. It would seem to me much more likely that in this family there is a hereditary vulnerability of the nervous system to syphilis and that, as the different members of the family became infected, they promptly developed symptoms in the nervous system. There is a recent theory that the secondary factor in the development of the parasyphilitic disease is some disturbance in the secretion of a ductless gland, particularly the thyroid. In this connection it is interesting to observe that two sisters of the patient had goiter and the patient's daughter has a goiter. The literature on the subject may be found in an article by Dr. Hans Barken[1] who quotes Stern as saying that the necessary triad for the development of the metasyphilitic diseases of the nervous system tabes and paresis is: a "dispositio paralyticans," a luetic infection and a pathologic functioning of certain ductless glands. Inasmuch as any special bodily constitution is probably the result of the action of the ductless glands, the triad is in reality a question of only two factors, according to this view. Maloney[2] calls

1. On the Simultaneous Occurrence and Interrelation of Pasedow's Disease and Tabes. Boston Medical and Surgical Journal, June 18, 1914.
2. Determinants of Tabes. New York Medical Journal, June 20, 1914.

attention to the probable importance of the chemical affinities of the tissues in the distribution of syphilitic lesions, and believes that these are influenced by the ductless glands.

The second point in connection with this case is that the patient absolutely denies syphilitic infection. He says that he has never had any signs of it and that a doctor at one time told him that he could not have syphilis without knowing it. This is an erroneous impression which seems to be widely prevalent. This patient is unquestionably infected; he has a double plus Wassermann reaction; and the diagnosis of tabes has been confirmed by several observers. I have had an opportunity of examining a number of cases of tabes and paresis in patients who strongly denied any knowledge of syphilitic infection. Among this number were several physicians, who might be expected to know, if anyone would, if they had syphilis. I have no reason to doubt their honesty when they say that they had never had any eruption, sore or other signs but the positive clinical symptoms and the blood and spinal fluid examinations showed the presence of syphilis beyond question.

This patient began having his symptoms of tabes in 1896, when he had sharp, shooting pains in various parts of the body. He noticed a difficulty in walking about five years ago and these have been the most prominent symptoms. The patient also shows Argyll-Robertson pupils, marked Romberg sign, absent knee and Achilles jerks, and loss of sense of motion and position in the feet. Some time after he noticed the disturbance in walking, he also noticed a continuous, very severe pain in the anterior portion of the dorsum of the foot. His physician told him that this pain was due to his disease. A layman, however, advised him to get an artificial arch for his foot; this he did, and he claims that he was very much relieved of the pain, and that for a year or more his gait steadily improved, without other treatment. It is well known that a hypotonicity present in tabes dorsalis leads to a flattening of the arches of the feet. This has two very important results: It not infrequently causes, or increases, tabetic pains; and it also interferes greatly, in fact it may be one of the chief factors of the difficulty in walking. It is highly important, therefore, in the treatment of these cases that flat arches or the turning in of the ankle should be attended to as a part of the treatment.

DISCUSSION.

Dr. Udo J. Wile: Dr. Camp has brought out two very interesting questions which are of exceeding interest not only to neurologists but also to syphilologists. The first is the possibility of their being special strains of the spirochete which have selective action for one or another of the systems. There is more than clinical evidence at the present time to bear out that contention. There is of course an analogy in bacteriology. One knows, for instance, that streptococcus of one form will give rise to erysipelas; and that a streptococcus which differs not in its morphology but simply in its cultural reactions will give rise to impetigo contagiosa; a third variety of streptococcus may give rise to severe throat infection, with peritonitis. Although we do not as yet know every thing concerning the life history of the spirochete, it seems probable that it will be found that there are certain strains which are more virulent than others and have an especial affinity for certain systems. It is a common clinical fact that patients infected from the same source will develop syphilis of one particular type. The point that Dr. Camp made that the vulnerability of the nervous system must be considered, is extremely important. There is one report, for example, from the German literature, of four men infected from the same woman, three of them developing general paresis and one tabes. The occurrence of central nervous system syphilis in husband and wife not uncommonly occurs and also seems to bear out this theory.

The spirochetes seen in the microscope in the living state also show various phenomena which tend to show that they are different regarding their individual resistance. Certain spirochetes, allowed to remain under the dark-field under favorable circumstances will outlive the other spirochetes in the same field. When certain chemical substances are placed in contact with these spirochetes, certain of the spirochetes will perish at once, others within ten minutes, while others are resistant to even three hours indicating an individual difference in virulence and viability. There not only seems to be a certain predilection for the nervous system, but the mucous membranes are involved in certain cases over other systems. The bones are very frequently the seat of the infection, to the exclusion of the other systems.

With regard to the belief that the ductless glands may play some role in the production of the so-called para-syphilitic infections, it is interesting to note that with the exception of the testis, the glands of internal secretion are seldom the seat of active syphilitic symptoms. Active syphilis of the hypophysis is almost unknown; syphilis of the thyroid is extremely rare; syphilis of the ovaries is exceptionally rare, thus it is an interesting paradox that the glands of internal secretion, if they have any bearing on the production of late nervous syphilis, seem to have a high resistance to the attacks of the spirochetes themselves.

Dr. C. D. Camp: I had hoped that Dr. Wile would bear me out in one point that I tried to make, i. e. that many of these case come to the clinic with tertiary syphilis having no knowledge of having had primary or secondary lesions. Of course it is amply proved that there are different strains of the spirochete, that the different strains affect different parts of the body quite regularly. But I think that Dr. Wile loses sight of one factor when he would explain such a family history as this one by an infection by a particular brand of spirochete. It is possible that two generations of the same family might be infected by the same strain but three generations seems improbable.

A CASE OF MARKED INDICANURIA IN A PSYCHOPATHIC PATIENT.

JAMES HOWARD AGNEW, M.D.

(From the Department of Internal Medicine, University of Michigan.)

The presence of coloring substances in the urine has attracted attention from the earliest times and both Hippocrates and Galen speak of a blue pigment in the urine. Many subsequent observers have noted this but it was not until 1857 that Schunck noted the constant presence of indican in the urine, named it and considered it identical with vegetable indican. In 1863 Hoppe-Seyler distinguished between the indican of the urine and vegetable indican and in 1873 Jaffé noted the increased output of indican in intestinal obstruction and subsequently its source from the indol of the large intestine was established.

Indol is produced by the bacterial decomposition of proteins containing the tryptophan group and most physiologic chemists doubt that it is formed in the body in any other way. Its chief source is therefore from the colon where such protein decomposition is going on, but it may be formed in a putrid abscess anywhere in the body. The indol is absorbed, carried to the liver where it is oxidized to indoxyl, combined with sulphuric acid and potassium to form potassium-indoxyl-sulphate or indican in which form it is excreted by the kidneys. Indican itself is colorless and it is when we treat the urine with acid and an oxidizing agent that indigo-blue is formed which is soluble in chloroform and is extracted in this way.

Indican is not present in the urine of the new born and often times not during the first few months of life. As to its significance the observation has been made by clinicians that persons in whom a very strong indican reaction can be obtained in the urine over a long period of time often suffer from nervous or dyspeptic disorders and it has been thought that there is some casual connection between the absorption of indol from the intestine and the development of functional nervous or nutritional derangements. However, this has never been placed upon a firm scientific basis. Herter (1) has shown that indol administered subcutaneously causes fatigue, headache, depression, twitching and sleeplessness; however, this was only with much larger doses than could possibly be absorbed in the same period of time. On the other hand many persons with these complaints have but traces of indican in the urine while many apparently healthy persons excrete large amounts. Herter (1) explains this by regarding the liver as a screen and says that if it does not remove indol promptly from the circulation symptoms will arise and it is this varying ability of the liver to conjugate indol that gives rise to the contradictory findings.

The relation of constipation to indicanuria is not constant and to produce indicanuaria constipation must cause stagnation of masses of undigested proteins or hydrolyzed proteins in the large intestine.

The amount of indican excreted by a healthy individual on a mixed diet is variously given at from two to ten mg. per twenty-four hours. A high protein diet will cause an increase in indican excretion and a protein free diet a diminution, although Moraczewski (2) found just the opposite. According to the theory advanced by Metchnikoff the growth of the Bacillus Bulgaricus hinders the growth of putrefactive bacteria in the intestine, thus preventing the formation of toxins which when absorbed cause arteriosclerotic changes and hence old age. If this be true there should be a diminished excretion of indican since the putrefactive fermentation would be lessened. The general findings have been that the feeding of Bacillus Bulgaricus has but little influence upon indican output but in going over the literature I was struck by the fact that there were but very few careful quantitative studies and it was therefore thought desirable to make such quantitative studies upon this patient.

The patient was in the service of Dr. Barrett at the State Psychopathic Hospital to whom I am indebted for the opportunity of making this study. The case is not presented from the standpoint of the clinical features but simply as a case of marked indicanuria. It will be sufficient to state that he was confused, generally depressed with occasional periods of excitement and was considered at the time to have some form of a toxic psychosis.

The patient C. F. male, aged 59, was admitted to the hospital Nov. 14, 1912 and died May 13, 1913. The history is practically negative, the present trouble of loss of strength, depression and worry dating from some family trouble occurring ten months previous to admission. The patient has lost thirty pounds in weight, is emaciated, but physical and neurologic examinations were practically negative. At this time the patient had an achlorhydria, the stool was negative and he was placed on a finely divided diet with hydrochloric acid after meals. The urine was negative except for the constant presence of a few granular casts until on January 26 it was noted that upon boiling the urine with nitric acid it became a deep purple color At this time he was referred to the Medical Clinic where it was found that this was due to a large amount of indican. On Feb. 3, the patient had a phenolsulphonephthalein excretion of 69 per cent. and the urea nitrogen was .32 g. per 1000 cubic centimeters of blood.

Twenty-four hour samples of urine were ex-

amined daily and the indican estimated according to the method of Ellinger (3) which is briefly as follows:

A measured sample of the twenty-four hour urine is precipitated with 20 per cent. lead acetate and a measured quantity of the filtrate treated with an equal amount of Obermayor's reagent. The indigo-blue thus formed is repeatedly extracted with chloroform, the chloroform distilled off, the residue dissolved in suphuric acid and titrated with a potassium permanganate solution whose oxidizing factor has previously been determined against pure indigo-blue. The results of these determinations together with notes on the diet and medication are shown in the table.

The plan of the test was four days of observation without in any way modifying the patient's diet or medication, followed by four days of active purgation with calomel and salts and another period of four days observation. This was then followed by four days during which the protein intake was greatly reduced and another period of three days with the original soft diet. The hydrochloric acid was then discontinued and three tablets of Bacillus Bulgaricus (Parke, Davis & Co.) were given after each meal for three days. After the lapse of three days the tablets were given again over a period of three days and a week later a flask of sterilized milk in which Bacillus Bulgaricus was subsequently planted was given to the patient on two days. The bacteria coagulated the milk and were present in pure culture producing a thick curd of not unpleasant taste. Quantitative estimations of indican were then continued at intervals and six weeks later daily feeding with 200 cubic centimeters milk cultures of Bacillus Bulgaricus were resumed and continued to the end of the observation which was twelve days before death. Toward the latter part of the observation the indican was estimated upon the combined urine of two successive days and where this has been done it is indicated by brackets. In these instances the amount of indican for any given day can be approximated by prorating according to the quantity of urine passed on that day.

It should be noted that the patient had been taking fifteen drops of dilute hydrochloric acid after meals since his admission to the hospital but that for six weeks previous to beginning the quantitative estimations he had taken no meat, his diet consisting of cereals, milk, potato, toast, eggs, custard, fruit, butter, sugar and olive oil at times.

It is seen that during the three months the patient was under observation there were many marked and sudden variations in the quantity of indican excreted for which there is no adequate explanation. However, there was a gradual lessening of the amount excreted and the last few examinations gave amounts of indican at the upper limits of normal but very much less than the amounts first found. When we attempt to draw conclusions from any particular form of medication or diet we find it is impossible.

During the preliminary period of observation there were marked variations followed by a fairly definite diminished indican excretion while the patient was being purged, which was in turn followed by the excretion of the largest amount observed at any one time—.3718 g. In going over the literature rather superficially I have not come upon a case reported where so large a quantity was excreted. Wang (4) reports a case of tuberculous peritonitis in which there was a daily indican output of .260 g.

Upon the day following the excretion of this very large quantity of indican, less than one-quarter of that amount was excreted, and following this there was a gradual but definite decrease in the indican excretion, not markedly influenced by the very low protein diet nor by the administration of Bacillus Bulgaricus tablets. The feeding with milk cultures of Bacillus Bulgaricus however appeared to have some effect for subsequently to that there was but one instance in which the indican excretion was more than 35 mg. and when the milk cultures were given daily the indican excretion ranged from 10 to 20 mg.

That large quantities of indican were not in this patient's urine previous to the first time it was noted seems assured as fifteen urine examinations had been made during the three preceding months with negative results except for casts. It may be that this was simply a wave of indicanuria which quickly reached its height and slowly subsided.

Herter (1) found that in dogs, injections of Bacillus Bulgaricus into the intestine caused a diminution of the intensity of the indican reaction of the urine. Moraczewski (2) found no change of indican output in patients fed with Bacillus Bulgaricus, nor did he find any relation between the indol of the feces and the indican of the urine.

At autopsy there was found a thrombophlebitis of the right renal, common iliac and femoral veins, embolism and thrombosis of the pulmonary vessels, purulent pneumonia, emphysema, general sclerosis, atrophy and passive congestion, and a cyst of the pituitary body.

It is impossible to draw any definite conclusions as to the effect of diet or medication upon the indican output from a single case and this is reported simply as a case of marked indicanuria.

Date	Amt. Urine in c. c.	Amt. Indican in grams	Diet	Remarks
1-31-'13	1550	.1023	Soft	Specific gravity 1.011. Few casts. No albumin. Bowels regular.
2- 1-'13	1800	.1121	Soft	Specific gravity 1.008. Hydrochloric acid after meals.
2- 2-'13	1500	.0697	Soft	Specific gravity 1.006. Hydrochloric acid after meals.
2- 3-'13	1770	.1404	Soft	Specific gravity 1.009. Hydrochloric acid after meals. Received Calomel grs. 2 and epsom salts, ounces 1.
2- 4-'13	840	.0313	Soft	Specific gravity 1.017. Hydrochloric acid after meals. Received one ounce salts.
2- 5-'13	900	.0356	Soft	Specific gravity 1.013. Hydrochloric acid after meals. Received one ounce salts.
2- 6-'13	1150	.0622	Soft	Specific gravity 1.016. Hydrochloric acid after meals. Received one ounce salts.
2- 7-'13	1800	.0848	Soft	Specific gravity 1.014. Hydrochloric acid after meals.
2- 8-'13	1325	.2088	Soft	Specific gravity 1.011. Hydrochloric acid after meals, Stool 1.
2- 9-'13	1050	.3718	Soft	Specific gravity 1.017 Stool, 1.
2-10-'13	1000	.0926	Soft	Specific gravity 1.014.
2-11-'13	900	.0895	Soft	Hydrochloric acid after meals. Stool, 1.
2-12-'13	1400	.0724	Very low protein	Hydrochloric acid after meals. Stool, 1.
2-13-'13	1340	.0554	Very low protein	Hydrochloric after meals. Stool, 1.
2-14-'13	1440	.0981	Very low protein	Hydrochloric acid after meals.
2-15-'13	700	.0705	Very low protein	Hydrochloric acid after meals. Very active.
2-16-'13	600	.0471	Light	Hydrochloric acid after meals. Stool 1. Not a 24 hour specimen.
2-17-'13	610	.0473	Light	Hydrochloric acid after meals. Only a 21 hour specimen.
2-18-'13	530	.0636	Soft	Stool 1.
2-19-'13	540	.0490	Soft	Received nine tablets B. Bulgaricus.
2-20-'14	975	.0603	Soft	Received nine tablets B. Bulgaricus. One stool.
2-21-'13	425	.0525	Soft	Received nine tablets B. Bulgaricus. One stool, not a 24 hour specimen.
2-22-'13			Soft	Much disturbed. Unable to collect urine until 2-25-'13.
2-25'13	1000	.0458	Soft	Very confused.
2-26-'13	800	.0477	Soft	
2-27-'13	420	.0539	Soft	Received nine tablets B. Bulgaricus. Complete 24 hour sample.
2-28-'13	480	.0509	Soft	Received nine tablets B. Bulgaricus. Complete 24 hour sample.
3- 1-'13 3- 2-'13	760 620	.0981	Soft	Received 7 tablets B. Bulgaricus.
3- 3-'13 3- 4-'13	1190 720	.1157	Soft	
3 -5-'13 3- 6-'13	430 980	.1085	Soft	Not a 24 hour sample.
3- 7-'13			Soft	Urine lost.
3- 8-'13 3- 9-'13	630 560	.0992	Soft	Not a 24 hour sample.
3-10-'13 3-11-'13	975 825	.0760	Soft	Not a 24 hour sample. Milk culture B. Bulgaricus
3-12-'13			Soft	Milk culture, B. Bulgaricus.
3-13-'13	370	.0176	Soft	Complete 24 hour sample. Marked twitching.
3-14-'13 3-15-'13	550 900	.0622	Soft	

Date	Amt. Urine in c. c.	Amt. Indican in grams	Diet	Remarks
4-12-'13	600	.0706	Soft	Has grown much weaker. Is taking no Hydrochloric acid.
4-13-'13	440			
4-19-'13	610	.0571	Soft	27 hour sample.
4-21-'13	300	.0357	Soft	
4-22-'13			Soft	Has grown weaker. Marked twitching. Test for Indican in blood negative.
4-26-'13			Soft	Milk culture B. Bulgaricus.
4-27-'13	390	.0180	Soft	Milk culture B. Bulgaricus. 14 hour specimen of urine.
4-28-'13	500	.0182	Soft	Milk culture B. Bulgaricus. 22 hour specimen.
4-29-'13	920	.0185	Soft	Milk culture B. Bulgaricus.
4-30-'13	380	.0107	Soft	Milk culture B. Bulgaricus. 24 hour specimen.
5- 1-'13	440	.0202	Soft	Milk culture B. Bulgaricus.

DISCUSSION.

Dr. C. D. Camp: This case is very interesting from the clinical standpoint. It is possible, I think, that many of the symptoms that the man showed were to be attributed to the cyst of the pituitary body which was unsuspected during life but was a very prominent feature in the autopsy findings. Whether disturbance of the pituitary body could have caused the indicanuria, it seems to me, is a very interesting question which might be further gone into.

Dr. James H. Agnew: In regard to Dr. Camp's remarks, I am not so familiar with the clinical aspects of the case. I was interested particularly from the standpoint of the indicanuria. It has been very definitely proven that thyroid feeding will cause an increase in the indican output but I have seen nothing regarding the effects of pituitary extracts upon indican output.

It seems rather strange, however, if the pituitary body had anything to do with this, that he should have such a large excretion and then such a sudden falling off. I am inclined to believe that the feeding with Bacillus Bulgaricus had nothing to do with this and that it would have fallen off without medication. Furthermore, it would seem that from the fifteen previous urine examinations, if there had been any marked indicanuria, it would have been noted. I believe a very practical point is that a single sample of urine tested for indican is practically valueless and that a twenty-four hour specimen should be used.

Dr. R. Bishop Canfield: Do you suppose that approaching death had any thing to do with it?

Dr. James H. Agnew: No; in approaching death with cardiac decompensation, the test for indican is unchanged. In uremia there is an increased excretion of indican and particularly indican in the blood.

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A CASE OF HYDROCEPHALUS.

Albert H. Beifeld, M.D.

(From the Department of Pediatrics, University of Michigan.)

This baby was brought to the Pediatric Service yesterday and is shown here this evening merely to demonstrate the size of the head. The baby is 21 months old, normal birth and normal family history. While the child's head was believed to be rather large at birth, the real enlargement was not noted until after six weeks and from that time until now a progressive enlargement has been observed. There is nothing to account for this increase in the size of the head, although it is not uninteresting to note that in the first month of the infant's life it was exposed to tuberculosis, the patient being the landlady in the house where the child lived.

The circumference of the skull is 64 cm.; the normal measurements at this age, 21 months, being about 40 cm. It is interesting to note the marked degree of ossification of the skull. In most cases of hypdrocephalus one expects a separation of the sutures and gaping of the fontanelles. In this case, however, the posterior fontanelle is almost closed, the anterior fontanelle measuring 9 cm. and the sutures firmly united. There is the usual pushing down of the eye-ball due to the forward and downward pressure upon the orbit. The reflexes are so markedly increased that the slightest touch will produce clonus. Lumbar puncture has not been done as we are having an apparatus made for the purpose of trans-illumination. With this we hope to observe the effect of puncture on the accumulation of fluid.

DISCUSSION.

Dr. D. M. Cowie: A great many of these cases come to the children's clinic. The problem is how to treat them. If lues is an etiologic factor it is possible that treatment for this condition may be of benefit. Surgical interference has brought about

varying results. In not a few cases of hydrocephalus, operation has proved a distinct benefit. The principle involved in the surgical care of these cases is drainage. This may be effected in several ways. If a case can be proved to be of the external type, drainage into the soft tissues of the head may suffice. Dr. de Nancrede operated one such case for me in this way. There was distinct drainage around the filagree of silver wire for a while. A second operation was advised but the patient passed from under our observation.

In the internal variety, drainage of the ventricles into the sinus or cisterna magnum has given encouraging results in several cases recorded in the literature. Simple tapping of the ventricles through the corpus callosom has been followed by relief in a few cases. A more complicated and extensive operation is that of drainage of the cerebrospinal fluid into the abdomen. This operation has to be done in two or three stages and is very difficult.

While the results following such operations on the whole have not been very encouraging I, never-the-less, believe that when we have such cases in private or hospital practices we should encourage operative measures. With improvement in operative methods and technic, as well as in methods of diagnosis it is not at all improbable that sooner or later something will be discovered to help certain groups of cases. There is certainly no medical treatment of any avail.

Dr. Beifield: In the shortness of time we have not had a report of the Wassermann. There is a belief that a large number of these cases are syphilitic. The child was treated with the inevitable protoiodid pills for quite a long time.

Dr. R. Bishhop Canfield: My experience in surgical treatment of these cases is limited to one case. In this case the patient's basal cystern was opened and drainage secured by means of a knotted silk ligature one end of which was passed through the dura and the other end carried downward under the deep neck muscle. We secured drainage for as long as the patient remained under observation and there were definite signs of improvement. The downward position of the eyes was somewhat improved. The child was able to feed itself solid food. It gained in intelligence. It developed several new words in its vocabulary, while under observation. It recognized its relatives and called them by some baby name, giving the relative always the same name. It showed therefore, signs of improvement. It seems to me that the greatest point is an early diagnosis, a diagnosis before the head has changed in its size so tremendously, and some definite drainage introduced before the ventricules have become so permanently dilated and the cortex so thin that there is no possibility of the child developing any mentality. It appears to me that with an early diagnosis, an early operation might be of service. There were one or two successful cases in which a gold tube has been introduced, one end into the torcular and the other end through the subdural space. In this way the pressure in the subdural space may be reduced to that of the torcular. The operation has been done a couple of times with some improvement.

A CASE REPORT.

Harold I. Lillie, A.B., M.D.

(From the Otolaryngology Clinic, University of Michigan.)

The case I wish to report tonight is that of a young man, twenty-three years of age, who entered the Neurological clinic three years ago, 1910, complaining of inability to open his mouth or chew his food and of weakness in the arms and legs.

Family History.—Father has asthma, the mother is a very nervous individual, the maternal grandmother is eighty years of age and has senile dementia.

The previous history shows the patient to have had two rather severe accidents, one supposed to have resulted in cerebral concussion, from which he recovered completely. He denies venereal infection.

The present trouble started six weeks previously with pains in hips and legs, followed by muscular weakness becoming so pronounced that he was unable to walk. Pain and weakness developed in upper extremities.

Neurologic examination, 1910, Dr. Camp: No absolute paralysis, no pain in nuscle masses. Movements painful. Tactile sensations not changed. No pain with pressure over nerve trunks. All muscles react to faradic current. Tendon reflexs prompt. Anesthesia of conjunctiva. Physical examination, negative; urine, negative.

He was treated with static spark and three weeks later discharged, very much improved, and remained so.

His second admission was in December 1913, when he complained about stiffness of the back and pains from hips to knees. No ataxia; no trouble with sight or hearing; no vomiting.

Neurologic examination, Dr. Camp: Conjunctiva anesthetic. No paralysis, atrophy or disturbance of sensation. There was a slight rigidity of spine, but no deformity. The rigidity was not absolute, however. This he says has developed so slowly he does not know when it could have started. It is variable. It does not affect the cervical region. He puts both arms above his head and holds them there with equal strength. Joints are negative. Wassermann, negative; urine, negative. Physical examination, negative.

The patient said that he had consulted a physician in Chicago for this same trouble and that after a careful examination, both physical and X-Ray, he was told he had arthritis deformans. His consultant recommended that his tonsils be enucleated.

Examination of the patient in Otology clinic revealed septic tonsils with enlargement of the anterior cervical glands. History showed repeated attacks of sore throat.

X-Ray examinations of spinal column, I will quote: "Bodies of the second, third, fourth and fifth lumbar well shown. Fifth is rather hazy and indistinct from superposition upon sacrum. There is no lipping, no opacities, no dislodgement or other evidence of disease of the centra. The posterior artifications are also normal.

We find no evidence of disease in this spine."

The patient was then transferred to the Otology clinic for tonsil enucleation, having been told his trouble would disappear if his tonsils were removed. The operation was performed under cocain anesthesia with very great difficulty. Although the patient said he experienced no pain, the instrument caused him to gag and cough and he would not keep his mouth open, despite the careful instructions. There was no post operative bleeding, and the next day he complained little of sore throat. On the third and fourth day he noticed his back was not so stiff. He apparently was delighted and was noticed in the ward bending over, in all directions. The movement became normal and patient was discharged.

This patient is interesting (1) because he is a type of hysterical patient which responds to well directed treatment. (2) Had he followed the advice of his Chicago consultant, the result would no doubt have been reported as a case of arthritis deformans cured by tonsil enucleation.

DISCUSSION.

Dr. C. D. Camp: I remember this patient very well because my attention was called to him recently. When I first saw him in 1910, the case showed nothing of special interest. As I remember, it was a case of hysterical paralysis of one or both arms. The condition was treated purely symptomatically, that is, by suggestion. The symptoms were so completely relieved that the patient left the hospital because he felt well. The patient returned some time later, three years, I think, and said that a diagnosis of rheumatoid arthritis of the spine had been made. An examination shortly after admission to the hospital pointed conclusively to the fact that the spinal trouble was also hysterical and that opinion was confirmed by his X-Ray examination. He was convinced that the spinal trouble would yield to a tonsilectomy and, inasmuch as he probably needed a tonsilectomy anyway, that seemed the most servicable way to treat him and he improved very rapidly after the tonsilectomy. Three or four days after, he showed me that he could touch the floor with his fingers without bending his knees. I think the point is that literature should be judged rather critically when we read accounts of minor operations being beneficial in arthritis or other obscure complaints.

A REPORT FROM THE CLINIC OF OPHTHALMIC SURGERY OF A SERIES OF OPHTHALMOSCOPIC STUDIES OF THE FUNDUS IN CASES OF NEPHRITIS.

Dr. George Slocum.

Instructor in Ophthalmology, University of Michigan.

Long before the discovery of the ophthalmoscope it was known that nephritis is often accompanied by visual disturbances, and as early as 1836 John Bright noticed that such disturbances are sometimes the earliest observed symptoms. The pathologic changes in the retina were described postmortum by Turk in 1850 and by Virchow in 1855.

When in 1851 Helmholz invented the ophthalmoscope, a new world of investigation was opened for the study of pathologic changes in the interior of the eye. Before the time of Helmholz's discovery many intraocular diseases remained more or less of a mystery, the changes produced by most of the intraocular diseases causing blindness being known only through histo-pathologic study. With the discovery of the ophthalmoscope, the interior of the eye in all its living physiologic activity was revealed and eager investigators commenced the study of the interior of the eye. The first published ophthalmoscopic studies of the retinal changes of nephritis were those of Heyman in 1856 and Liebreich in 1859. It was not a long time before the study of the fundus so fascinated a number of able men, that a great wealth of material was accumulated, and descriptions of the most careful and painstaking series of observations have constantly been added until it seems next to impossible to discover any conditions which have not been ably described by earlier observers. While the present series of observations were conducted with a full knowledge that the conditions studied have already been described in the minutest detail, accompanied in many instances by the most beautifully executed colored drawings and paintings, the study has been made in the hope of throwing more light upon the relation between the different types of nephritis and the associated ophthalmoscopic picture. It has often been stated and many believe that the type of ocular inflammation or degenerative process seen in certain general diseases varies with the type of histologic structure involved in the general process; for instance in lues when collagenous structures are invaded in the eye, is not the same class of tissues involved within the cranium; when the vascular structures are involved, may we not look for an intracranial involvement of the choroid plexus or pial tissue; or, in cases of neuroretinitis or papillitis where the brunt of the attack seems to be centered in the nervous structures, may we not be able to find that the changes are similar to those which are found in the interior of the brain or in the spinal cord? It has also often been observed that a relation seems to exist between the type of fundus changes found and the type of systemic condition having an etiologic relation, as for instance in cases of nephritis. It was with the purpose of studying these relations in this class of cases that the present series of observations was undertaken. The main questions considered are first to what extent do the exudative and hemorrhagic retinal changes seen in the acute forms of nephritis correspond to the pathologic changes found

in the kidneys? Second: Is there a constant or characteristic relation between the retinitis associated with parenchymatous nephritis and the pathologic changes in the kidneys? Third: Can a characteristic relation be established between the vascular changes almost invariably accompanying the chronic interstitial type of nephritis and the vascular changes frequently seen in the retina? Fourth: What other relation may exist between the fundus changes and the pathologic manifestations?

The familiar classical picture of albuminuric retinitis presents a glistening white change in the macular region having a radiating spoke like a star shaped arrangement, often associated with hemorrhages of varying types in the neighborhood of the temporal vessels or in the maular region. This type of retinitis is present in the late stages of about 30 to 50 per cent. of contracted kidneys. It is rare indeed that any condition of the retina develops having the typical features of this form of retinitis, that cannot be traced directly to kidney disease or hypertension. Such macular changes are degenerative in character, probably due to atrophic changes in the macula following the macular edema of an earlier stage. When we recall the radiating anatomic arrangement of the retinal elements in the macular area in Henle's horizontal layer, the fact that an edema, an exudate, hemorrhagic or inflammatory changes in this region take on a radiating character, as following the lines of least resistance is at once satisfactorily explained. Later atrophic changes would cause the radiating pathologic process to become conspicuously white as well as star like in arrangement. There are a certain number of albuminuric retinitis cases which are characterized by small white dots and spots in the macular region not having a typical radiating arrangement. To determine, if possible, the type of vascular change present in these two conditions was one of the objects of this study.

Hemorrhages may be present sooner or later in practically all cases of albuminuric retinitis. Indeed, some of the permanent changes found in the retina are due to the failure of absorption of extravasated blood with later organization of fibrin and blood pigment changes. The appearance of the fibrin is at first fluffy, that is, immediately after absorption of migration of the blood pigment, resembling an inflammatory exudate; gradually changing through successive stages, finally flattened atrophic patches appear, remaining bordered, perhaps, by irregular patches or degenerated blood pigment which cannot be distinguished ophthalmoscopically from retinal pigment. Hemorrhagic changes, however, are present in many forms of retinitis not dependent upon kidney disease. That hemorrhages should be more likely to occur in cases of the interstitial type one might expect when one remembers that vascular changes are such a prominent feature in the pathology of interstitial nephritis. The type of hemorrhages, other things being equal, would depend somewhat upon the type of vessels involved. When the fine capillaries are affected, associated hemorrhages in the retina would be more likely to be present in the outer vascular plexus of the retina. Such hemorrhages would usually be small, rounded in character, and because of the histology of the middle layers of the retina, would have a tendency to extend vertically rather than horizontally. The resulting hyaline or fatty changes lead to marked vertical changes associated with cystoid spaces filled with hyaline or fibrous material.[1] In the others where the small arterioles are involved, the hemorrhages would become prominent in the inner vascular plexus in the nerve fiber layer, and would follow the line of least resistance along the interfasicular clefts in the inner fiber layer and therefore assume a flame like shape. Still other hemorrhages and exudates occur between the lamina vitrea choroidea and the retina producing small local detachments. The larger hemorrhages are usually subhyaloid, that is between the retina and the vitreous. Inasmuch as such hemorrhages are sometimes seen in cases presenting no discoverable systemic disturbance their diagnostic importance is not as well established.

Neuroretinitis, papillitis, or even choked disc are sometimes seen in kidney disease, more especially perhaps in acute types such as the acute nephritis of scarlet fever or in the nephritis of pregnancy in which the changes are often quite characteristic. In the more acute types large exudative spots of considerable size may appear, hemorrhages are relatively fewer, the retina is deeply edematous, becomes muddy, is locally detached, loses its transparency, and fine granular opacities are often present in the media. In the series of cases examined, the acute type is present in two cases only. Retinal changes associated with nephritis may be classified as follows: 1. Vascular changes; (a) Increased arterial tension as shown by arteriovenous compression, the veins being compressed by the more rigid overlying artery, resulting in local dilation of the vein distal to the compression. (b) Fine tortuosities of the arteries and veins, corkscrew vessels particularly in the macular region with or without small hemorrhages. (c) Degeneration of the walls of the arteries as shown by the broadening of the arterial reflex stripe, in endarteritis or thickening of the perivascular lymph sheathes, as seen in periarteritis, changes which often advance to the extent of the formatun of the so-called silver wire vessels in which

1. Parson's Pathology P. 1298.

a portion of the blood stream is entirely obscured by the opaque degenerated vessel wall. 2. Neuro-retinitis, and optic neuritis with slight detachment of the retina in the neighborhood of the disc may be due more or less directly to toxic substances which have accumulated in the system because of imperfect elimination, or perhaps in some cases of choked disc to an increase of intracranial pressure. 3. Hemorrhagic retinitis, especially if bilateral and accompanied by exudative changes or edema. 4. Small white spots in the retina near the disc or in the macular region especially when bilateral and accompanied by other retinal changes. 5. Punctate retinitis in the macular region bilateral, especially when associated with edema or hemorrhages. 6. Glistening white spots in the macular region or between the macula and the disc having a radiating arrangement centered in the macula, a late change associated with chronic types. 7. Late changes such as secondary optic atrophy or retinal atrophy following a marked neuroretinitis or papillitis in one of the acute exanthemata or in the albuminuric retinitis seen in pregnancy. 8. Choroidal changes dependent upon vascular changes similar to those which take place in the retinal vessels associated with hemorrhages in the choroid which are sometimes present in albuminuric retinitis.

Vision is impaired in albuminuric retinitis in proportion to the size of area, and according to the locality involved in the pathologic process. As would be expected, exudative and degenerative types in the macular region give the greatest amount of immediate impairment; inflammatory types may cause an acute impairment of vision which in severe cases becomes more marked as atrophic changes supervene.

I have divided the cases presented in this report into five classes:

a. Chronic Interstitial Nephritis.
b. Chronic Nephritis.
c. Hypertension.
d. Acute Nephritis.
e. Miscellaneous.

They are tabulated below grouping the symptoms to facilitate comparison of the various features.

SERIES A.

Chronic Interstitial Nephritis.	Sex	Age	Vision O D	Vision O S	Ocular Findings.
1. C. G. 6-12-12. Medical Diagnosis: Chronic interstitial nephritis. Hypertension. Arterial sclerosis. Heart enlarged. Urine: Trace albumen, fine granular casts, B. P. 200 to 240. Symptoms: Headache, dyspnea; occasional edema of legs.	M	75	c. f.	c. f.	O. D. Fusiform venous dilations; many rounded flame shaped hemorrhages, one large subhyaloid hemorrhage. Marked edema of the disc and retina; retinal detachment down and temporally. Choroidal vessels sclerosed O. S. Large detachment lower third of retina; exudates and macular changes. Lenses cataractous.
2. C. H. 10-22-12. Medical Diagnosis: Advanced chronic interstitial nephritis. Heart enlarged and hypertrophied. Urine: Large amount of albumen, hyaline and granular casts. B. P. 195 to 220. Symptoms: Extreme dyspnea on exertion; some edema of legs.	M	44	5/4	5/4	O. D. Periarteritis; endarteritis; arteries small; veins irregular in caliber. Retina edematous; subretinal exudates; hemorrhages and exudates in retina. Edema of macula. O. S. Silver wire artery; arteriovenous compression dilation. Hemorrhages in the retina rounded and flame shaped.
3. C. J. 12-2-12. Medical Diagnosis: Chronic interstitial nephritis. Uremia: Dilated heart; hydrothorax; radial and temporal vessels sclerosed. Urine: Large amount albumen, granular and hyaline casts. B. P. 150-190. Symptoms: Cheyne-Stokes respiration; dyspnea.	M	48	5/10	5/6	O. D. Marked endarteritis; arteriovenous compression dilation. Marked retinal edema; flame shaped hemorrhages; exudative changes. Minute exudative spots in the macula. O. S. Rounded hemorrhages, glistening white spots, a few exudative changes and slight pigment change in macula. Tortuosities of macular vessels; one macular vessel silver wire; O. S. same as in O. D.
4. L. H. 12-13-12. Medical Diagnosis: Interstitial nephritis chronic, hypertension. Urine: Albumen, large amount, granular casts. B. P. 205 to 175. Heart slightly enlarged. Symptoms: Dyspnea, headaches, nausea vomiting, dizziness, blurred vision.	F	43	6/6	6/6	O. D. Endarteritis; arteriovenous compression; veins tortuous. Macula edematous Retina edematous. O. S. Disc edematous, otherwise the same as O. D.
5. B. J. 12-27-12. Medical Diagnosis: Mental derangement due to vascular change. Urine: Large amount albumen, granular casts. B. P. 210 to 250. Radials sclerotic. Mental confusion.	M	?	4/20	4/20	O. D. Discs edematous. Arteries contracted; endarteritis Choroid atrophic. No exudate, hemorrhages or atrophic changes.
6. C. D. 3-21-14. Medical Diagnosis: Chronic interstitial nephritis. Arterial sclerosis; myocardial insufficiency. Heart enlarged. Urine: No albumen, a few hyaline casts. B. P. 195 to 155. Symptoms: Headaches, nausea and vomiting, dyspnea, edema of hands and under eyes.	M	53	5/7	5/10	O. D. Periarteritis; endarteritis; arteriovenous compression dilation. One or two small hemorrhages near the macula. Two small exudates in retina; retina edematous. O. S. Much the same as O. D. also macula edematous but no exudates or hemorrhages.

SERIES A—Concluded.

Chronic Interstitial Nephritis.	Sex	Age	Vision O D	Vision O S	Ocular Findings.
7. E. J. 4-9-13. Medical Diagnosis: Chronic interstitial nephritis. Tachycardia; uremia; heart enlarged; systolic murmurs radials sclerosed. Urine: Albumen, small amount and not always present, few casts; phenosulphen-test, elimination slow. B. P. 245 to 225, Hgb. 60 per cent. Urea in blood 2.02? Wassermann negative. Symptoms: Dizziness; occasional headache; dyspnea on exertion; swelling of ankles.	M	45	5/10	5/4	O. D. Disc edematous and congested. Marked endarteritis; slight perarteritis. Retina edematous especially toward the macula; rounded hemorrhages; flame shaped hemorrhages; atrophic retinal changes, white patches, many glistening exudative changes in the retina, small and scattered. Fine white dots and points in macula; exudates along walls of vessels. O. S. Disc edematous and congested. Perarteritis; marked endarteritis; silver wire arteries; vessels tortuous; arteriovenous compression dilation. Atrophic retinal changes, less marked than in O. D. Exudates less numerous but arterial changes more advanced.
8. E. N. 4-21-14. Medical Diagnosis: Chronic hypertension; nephritis. Urine: Albumen, faint trace, no casts; phenosulphon elemination rapid. B. P. 242 to 195 W. B. C. 11, 370 R. B. C. 4,690,000, blood urea .44 g. per liter. Symptoms: Headache; poor vision; pain in the heart.	F	47	5/6	5/15	O. D. Marked arteriovenous compression. Retinal edema. Central choroidal changes. O. S. Nerve head edematous; marked arterio venous compression; retina edematous; some exudative spots above the macula. A few glistening white spots between the macula and the disc, central choroidal changes.
9. W. McG. 4-24-13. Medical Diagnosis: Arterial sclerosis; interstitial nephritis; hypertension; heart enlarged; radial thickened. Urine: No albumen, a few granular casts; phenosulphon elimination good. B. P. 170. Symptoms: Severe precardial pain.	M	54	5/4	5/4	O. D. Disc congested and edematous. Veins engorged; marked arteriovenous compression dilation; arteries tortuous, irregular in caliber and show endarteritis. Retina edematous. Macula edematous. O. S. Endarteritis more marked, otherwise practically same.
10. J. L. 6-9-13. Medical Diagnosis: Chronic interstitial nephritis, hypertension, cardiac insufficiency. Heart slightly enlarged, faint systolic murmur. Urine: Albumen, moderate amount, no casts; phenosulphon. elimination very slow. B. P. 212 to 180. Symptoms: Dyspnea on exertion.	M	55	6/12	6/30	O. D. Nerve head edematous. Several whitish areas of infiltration of the retina near disc border temporally. Arteries contracted. Retina edematous. Up and nasally from the disc. hemorrhages and whitish, areas of infiltration. Macula edematous. O. S. Disc edematous. Arteries contracted. Several fine hemorrhages and small deposits (old hemorrhages) in temporal retina.
11. J. S. R. 12-9-13. Medical Diagnosis. Chronic interstitial nephritis; chronic hypertension. Heart slightly enlarged; radial thickened; extra systoles. Urine: Definite trace albumen, many hyaline and granular casts; phenosulphon. elimination slow. B. P. 190 to 155. Blood urea .75 gm. per liter. Symptoms: Headaches, spots before eyes, short of breath, edema of feet.	M	65	5/5	5/5	O. D. Disc edematous. Arteries irregular in caliber; endarteritis; partial silver wire artery; marked arteriovenous compression dilation. Retina edematous. O. S. Disc edematous. Arterial changes same as O. D. only more general and advanced; arteriovenous compression dilation more marked. One small linear hemorrhage above disc. Corkscrew macular vessels; macula edematous.
12. C. W. B. 6-24-13. Medical Diagnosis: General arterial sclerosis; chronic nephritis, secondary. Heart slightly enlarged; systolic murmur; radials sclerotic. Urine: Definite trace albumen; many hyaline and granular casts. B. P. 190 to 160. Hgb. 62 per cent. Symptoms: Principally those of chronic gastritis.	M	67	3/60	5/60	O. D. Lenticular opacities. Disc edematous. Endarteritis; veins irregular in caliber. Retina edematous. O. S. Fine lenticular opacities; a few vitreous opacities. Disc edematous. Endarteritis; vessels irregular in caliber. Retina and macula edematous. One small silver wire artery nasally; arteriovenous compression dilation.
13. J. V. 8-23-13. Referred to Medical clinic; diagnosis chronic nephritis, arterial sclerosis, mitral regurgitation. Greatly enlarged heart, harsh systolic murmur. Urine: Albumen negative at first, later trace hyaline casts, bacteria. B. P. 200 to 170 Wassermann negative. Symptoms: Poor vision; swelling under eyelids; dyspnea on exertion.	M	74	1/60 later. 1/60	6/60 3/60	O. D. Slight lenticular opacity. Periarteritis; veins irregular in caliber; arteriovenous compression dilation. Very many flame shaped, linear and rounded hemorrhages generally small in size in both retina and macula. Exudative changes (old hemorrhages?); choroidal changes in the retina and the macula. Retinal edema; slight retinal detachment. Some glistening white spots in the macula. O. S. Corneal opacities. Fundus details not clearly seen. Some peripheral pigmentary retinal changes. Hemorrhages and exudates in the macula.
14. T. B. 9-25-13. Medical Diagnosis. Chronic interstitial nephritis; hypertension; hypertrophied heart, vessels sclerotic. Urine: Large amount of albumen with hyaline and granular casts; phenosulphon elimination slow. B. P. 195 to 180 W. B. C. 8,500. R. B. C. 3,730,000. Blood urea .89 grm. per liter. Wassermann negative. Symptoms: Failing vision; headaches; dyspnea on exertion; edema of the ankles.	M	48	5/20	5/30	O. D. Disc swollen and edematous. congested. Veins engorged; arteries small; endarteritis. Retina congested, edematous and contains several hemorrhages and exudates. Hemorrhages in the macula typical; partial radiating glistening white macular star. O. S. Disc hyperemic, swollen 1½ to 2 diopters. Endarteritis. Many hemorrhages. Many minute white spots about the disc. Macular hemorrhage; glistening white macular spots, slightly radiating.

SERIES A—Continued.

Chronic Interstitial Nephritis.	Sex	Age	Vision O D	Vision O S	Ocular Findings.
15. F. L. 12-3-13. Medical Diagnosis: Chronic interstitial nephritis; hypertension; arterial sclerosis. Heart enlarged, systolic murmurs. Urine: Considerable amount albumen with hyaline and granular casts; phenosulphon elimination poor. B. P. 270 to 220. Urea .72 gm. per liter. Symptoms: Vomiting in A. M.; dyspnea on exertion; W. B. C. 7,750, R. B. C. 4,810,000.	M	50	5/12	5/15	O. D. Disc swollen 4 diopters, swelling extending some distance about the disc. Vessels are tortuous; endarteritis; periarteritis; arteriovenous compression. Many hemorrhages and exudative spots. O. S. Practically the same as O. D. in every respect.
16. W. L. 1-29-14. Medical Diagnosis: Chronic interstitial nephritis; hypertension. Heart enlarged, systolic murmur; mitral insufficiency. Urine: Considerable albumen with granular casts. B. P. 200 to 225. Blood urea .82 gm. per liter. W. B. C. 5,100, R. B. C. 4,630,000. Symptoms: Dizziness, loss of consciousness, dyspnea on exertion, edema of the ankles.	M	63	5/6	5/6	O. D. Disc swollen 2 diopters. Arteries irregular in caliber; endarteritis; arteries contracted; arteriovenous compression. Vetina edematous. Macular vessels tortuous; macula has granular changes. O. S. Disc edematous. Vascular condition the same as O. D.

SERIES B.

Chronic Nephritis.	Sex	Age	O D Vision	O S Vision	Ocular Findings.
1. G. M. 12-12-12. Medical Diagnosis: Chronic nephritis; secondary contracted kidney, interstitial type. Heart enlarged. Urine: Albumen, large amount; phenosulphon. elimination slow. B. P. 250 to 216. Symptoms: Headaches; short of breath; vomiting; edema lids and legs.	F	26	5/7⅔	5/7½	O. D. Nerve head swollen 4 diopters. Hemorrhages about the disc. Marked periarteritis; arteriovenous compression dilation. Retina edematous in which tortuous veins are embedded; veins engorged. Macular vessels cork screw like; beginning star shaped figure. O. S. Condition practically same as O. D., swelling same.
2. W. H. M. 1-16-13. Medical Diagnosis: Subacute parenchymatous nephritis. Heart enlarged. Urine: Large amount albumen, granular casts; phenosulphon. rather rapid elimination. B. P. 150. Symptoms: Pain in the back; nervous, restless.	M	44	5/6	5/6	O. D. Macular region slightly granular otherwise negative. O. S. Slight periarteritis and endarteritis. Macular vessels slightly tortouos; macula slightly granular, otherwise negative.
3. S. B. G. 3-10-13. Medical Diagnosis: Chronic nephritis. Heart enlarged; systolic murmur, radials thickened. Urine: Trace albumen, granular casts; phenosuphon. rather rapid elimination. B. P. 160 to 190. Symptoms: Markedly sleepy, some dyspnea on exertion, slight edema of legs.	M	48	5/7½	5/7½	O. D. Disc congested edematous. Veins engorged, arteries tortuous; perivasculitis; arteriovenous compression. Retina edematous. Some slight choroidal changes. O. S. One large retinal hemorrhage, subhyaloid, otherwise same as O. D.
4. A. S. R. 3-20-13. Medical Diagnosis: Chronic nephritis, secondary contracted kidney (interstitial type). Heart enlarged, systolic murmur. Urine: Large amount albumen, granular and hyaline casts; phenosulphon. rather rapid elimination. B. P. 225 to 186. Marked edema over the whole body, dyspnea at night, palpitation.	F	46	5/5	5/4	O. U. Retina slightly hyperemic. A few scattering minute white points in the macula. Possibly slight endarteritis.
5. J. C. 4-2-13. Medical Diagnosis: Acute exacerbation of chronic nephritis. Heart enlarged, radials sclerosed. Urine: Albumen trace, few hyaline casts; phenosulphon. elimination moderately retarded. B. P. 168 to 142. W. B.C. 12,700, R. B. C. 4,200,000. Wassermann negative. Urea blood .68 gm. per liter. Symptoms: Headaches intense, dizzinsss, dim vision, nausea and vomiting.	M	50	6/15	6/12	O. D. Disc swollen I. D. Veins engorged and tortuous and irregular in caliber; arteriovenous compression dilation. Retina edematous; small hemorrhages below macula; corkscrew vessels in macula. O. S. Disc swollen 3 diopters. Veins markedly tortuous, engorged and irregular in caliber; arteriovenous compression dilation. A few glistening white spots in the macula. Endarteritis of the central artery. Edema of the macula O. U.
6. A. M. N. 4-4-13. Medical Diagnosis: Chronic nephritis, late stage. Cardiac hypertrophy, mitral regurg., systolic murmur, capillary pulse. Urine: Large amount albumen, granular casts; phenosulphon. very slow elimination. B. P. 180 to 204 W. B. C. 25,700, R. B. C. 4,400,000 Hg. 55 per cent. Blood urea high .80 gm. per liter. Symptoms; Nausea, vomiting, dyspnea palpitation, edema legs and feet. (Died in ten days.)	M	47	6/5	6/5	O. D. Periarteritis; periphlebitis; vessels tortuous; marked endarteritis; arteriovenous compression. Retina edematous; several small hemorrhages; retinal sclerotic change above macula. Macula granular and edematous. O. S. Marked perivasculitis; arteries very tortuous; endarteritis, arteriovenous compression. Retina hyperemic marked edema. Macula edematous with beginning sclerotic changes.

SERIES B—Concluded.

Chronic Nephritis	Sex	Age	Vision O D	Vision O S	Ocular Findings.
7. D. D. Van A. 4-4-13. Medical Diagnosis: Chronic nephritis. Cardiac insufficiency, enlarged heart, extra systolic murmur. Urine: Large amount of albumen, fine granular and hyaline casts; phenosulphon. very slow elimination. B. P. 170 to 155. Blood urea .38 gm. per liter. Wassermann negative. Symptoms: Nausea and vomiting; dyspnea on exertion. Palpitation. (Died in 3 mo.)	M	58	5/5	5/4	O. D. Vessels tortuous. Retina edematous; many small glistening subretinal spots in macula. Macula edematous; a few fine central choroidal changes. O. S. Disc edematous. Large flame shaped hemorrhage below and nasally. All the vessels contracted and tortuous; arteriovenous compression dilation. Macula edematous and granular; whitish subretinal spots in macula. Choroid granular below macula.
8. A. L. G. 4-16-13. Medical Diagnosis: Chronic parenchymatous nephritis (mild.) Urine: Albumen, small amount present, hyaline and granular casts; phenosulphon. elimination very good. W. B. C. 15,300, R. B. C. 4,100,000 Hgb. 80 per cent. Symptoms: Headaches, sleepy.	M	29	5/5	5/5	O. D. Slight endarteritis; veins somewhat engorged, perivasculitis. Retinal edema; arteriovenous compression. O. S. Disc edematous. Practically the same as O. D.
9. W. W. 4-28-13. Medical Diagnosis: Chronic nephritis; cardiac insufficiency; marked anemia. Heart enlarged, systolic murmur; radials slightly thickened. Urine: No albumen, few granular casts; phenosulphon. elimination very slow. B. P. 190. W. B. C. 12,150 R. B. C. 3,450,000 Hgb. 27 per cent. Blood urea .53 gm. per liter. Symptoms: Dizziness, blurred vision abdominal pain, diarrhea, edema of legs dyspnea on exertion.	M	58	5/5	5/12	O. D. Disc swollen and edematous. Marked arterial and venous pulsation; veins engorged and irregular in caliber; arteriovenous compression. Retina edematous. Cork screw macular vessels; macula edematous. Diffuse choroidal changes in periphery. O. S. Disc slight edematous. Veins irregular in caliber; arteriovenous compression dilation, endarteritis. Retina slightly edematous.
10. J. E. M. 7-14-13. Medical Diagnosis: Chronic parenchymatous nephritis, secondary contracted kidney, unemia. Heart enlarged. Urine: Large amount of albumen, no casts; phenosulphon. no elimination in 2 hours. B. P. 160 to 148. Blood not examined. Symptoms: Dyspnea with cough, eyes puffy in A. M., edema of ankles.	M	24	5/6	5/6	O. D. Disc edematous with exudates; disc swollen about 1 diopter. Marked endarteritis and periarteritis. White spots about the disc (remains of old hemorrhages.) Retina edematous. Typical radiating white star like figure in the macula. O. S. Disc markedly edematous, swollen 1 diopter. Arteries irregular in caliber; marked endarteritis and perivasculitis; arteriovenous compression dilation. Many minute mottled whitish changes in the retina between the disc and the macula where they have a radiating arrangement. Retina edematous.
11. J. A. T. 7-31-13. Referred to Medical clinic; diagnosis; Chronic nephritis; hypertension. Heart enarged; emphysema of lungs. Urine: Albumen present with granular and hyaline casts. B. P. 180 cyst. 140 dias. Symptoms: Dizziness; dyspnea on exertion.	M	43	5/4	5/4	O. D. Disc is edematous. Arteriovenous compression. Retina and macula edematous. O. S. Periarteritis; arteriovenous compression; exudates near superiar nasal vessels. Retina edematous.
12. N. B. 2-12-14. Referred to Medical clinic. Diagnosis: Diabetes mellitus; chronic parenchymatous nephritis. Enlarged heart. Urine: Considerable albumen and some sugar. B. P. 170. Symptoms: Excessive thirst; dyspnea on exertion; swelling of feet.	F	63	1/60	5/20	O. D. Nearly mature senile cataract, fundus reflex, no details. O. S. Incipient cataract. Disc congested. Arteries contracted; arteriovenous compression dilation marked. Fundus edematous. Numerous hemorrhages. Portion of radiating white spot in macula and down.

SERIES C.

Hypertension	Sex	Age	Vision O D	Vision O S	Ocular Findings.
1. M. C. 12-19-12. Medical Diagnosis: Hypertension. Urine: Albumen, negative, no casts. B. P. 210 to 140, systolic heart murmurs. Symptoms: Dizzy spells; unconscious spells; headaches; dyspnea on exertion; edema of lids and ankles.	F	48	5/5	5/6	O. D. Disc hyperemic. Retina hyperemic and edematous; one small hemorrhage. Arteriovenous compression slight endarteritis. Small exudate in macula. O. S. Disc more hyperemic. Macula edematous. Endarteritis; tortuous arteries and veins; no hemorrhage; one exudative change below macula (old hemorrhage?)
2. J. R. 12-30-12. Medical Diagnosis: Chronic hypertension. Urine: Albumen, faint trace, few hyaline casts. B. P. 210 to 160. Heart enlarged, systolic murmurs. Symptoms: Headaches; dyspnea; ankles edematous.	F.	59	5/20	5/20	O. D. Incipient cataract. Discs congested. Smaller vessels show silver wire characteristics; arteriovenous compression dilation marked. Veins markedly tortuous. Retina edematous. Scattering minute choroidal changes. O. S. two small flame shaped hemorrhages near the macula; macula edematous, otherwise practically the same as O. D.

SERIES C—Concluded.

Hypertension	Sex	Age	Vision O D	Vision O S	Ocular Findings.
3. S. N. 4-10-13. Medical Diagnosis. Hypertension (chronic nephritis?) Heart enlarged, radial slightly thickened. Urine: No albumen nor casts. Phenosulphon. elimination fair. B. P. 188 to 154. W. B. C. 8,300, R. B. C. 4,940,000. Symptoms: Dizziness, vomiting and nausea A. M.	M	49	6/20	6/20	O. D. Disc edematous extending below into edematous area in retina in which inferior temporal artery is buried. This area is elevated about 3 D, probably slight detachment. Whole retina hyperemic and markedly edematous. Macula edematous. Localized chorio-retinal change down and temporally. O. S. Periarteritis. Retina congested and markedly edematous. Macula edematous. General characteristics about the same as O. D. Appearance of fundus somewhat resemble leukemic retinitis.
4. W. J. M. 5-22-13. Medical Diagnosis: Hypertension; arterial sclerosis; prostatic hypertrophy. Radial thickened. Urine: No albumen, hyaline and granular casts. Phenosulphon. elimination good. B. P. 180. Symptoms: Patient disorientated, poor memory.	M	57	5/7½	5/7½	O. D. Many vitreous opacities. Disc congested and edematous. Veins engorged, somewhat tortuous and irregular in caliber; arteriovenous compression dilation; marked endarteritis. Retina edematous; several white spots in the retina irregularly arranged mostly bordering the macula. Small hyaline dots in the macula; macula edematous. O. S. Disc edematous and hyperemic. Endarteritis; some perivasculitis; arteriovenous compression dilation.
5. A. McD. 5-22-13. Medical Diagnosis: Chronic hypertension; arterial sclerosis. Cardiac arhythmia, extra systole. Radials beaded; brachials sclerotic. Urine: No albumen, no casts. B. P. 235 to 170. Symptoms: Vertigo.	M	78	5/20	5/7½	O. D. Lenticular opacities. Disc edematous. Veins irregular in caliber. Retina markedly edematous. Macula edematous. O. S. Arteriovenous compression dilation. Retina edematous. Macula hyperemic and granular.
6. T. A. S. 10-22-13. Medical Diagnosis: Hypertension; arterial sclerosis; chronic nephritis. Enlarged heart, systolic murmur. Urine: Albumen, negative; hyaline casts; phenosulphon. elimination fair. B. P. syst. 232, diast. 185. Wasserman negative. Symptoms: Unconscious spells; headache; some dyspnea on exertion. W. B. C. 9,650, R. B. C. 4,810,000.	M	40	5/5	5/5	O. D. Disc hypermic. Veins engorged and tortuous, periarteritis, endarteritis; arteriovenous compression dilation. Retina edematous; area of retinal change with swelling near disc; localized detachment. White spots above the disc and the superior macular region. Two small linear hemorrhages. O. S. Disc swollen 1 diopter, edematous and hyperemic. Perivasculitis; small hemorrhage near the disc; veins engorged: temporally the vessels are tortuous; arteriovenous compression dilation. Retina edematous, some scattering hemorrhages and old hemorrhagic areas. Macula edematous.
7. B. L. 1-11-14. Referred to Medicine. Medical Diagnosis: Myocardial insufficiency; hypertension; arterial sclerosis (chronic interstitial nephritis?) Heart enlarged. Urine: Slight trace albumen, sp. gr. 1006. B. P. 200. Symptoms: Headache; vomiting; dyspnea on exertion.	F	55	6/60 Wl. 6/60	5/20 C. 6/10	O. D. Disc edematous. Endarteritis and periarteritis; vessels tortuous; arteriovenous compression. Many small exudates and hemorrhages most numerous in the macula; macula edematous. O. S. Disc edematous. Veins engorged; arteriovenous compression dilation. Old thrombosis of inferior temporal veins, walls showing only as atrophic thin white lines, branches traceable. Some sclerotic changes in choroidal vessels.

SERIES D.

Acute Nephritis.	Sex	Age	Vision O D	Vision O S	Ocular Findings.
1. W. H. 3-13-13. Medical Diagnosis: Acute nephritis. Paralysis from anterior poliomyelitis, attack 4 years ago. Rapid heart. Urine: Albumen, present; no casts. B. P. 125. W. B. C. 14,500, R. B. C. 4,600,000 Hgb. 75 per cent. Symptoms: Has spots before eyes and headaches.	M	19	5/4	5/4	O. D. Nerve head congested and edematous. Marked perivasculitis; veins engorged; arteriovenous compression dilation. Mucula edematous. O. S. Disc more edematous. Some endarteritis: small veins tortuous. Condition practically the same as in O. D.
2. M. J. 6-3-14. Medical Diagnosis: Acute nephritis following mastoid operation for mastoiditis and sigmoid phlebitis. Urine: Normal before operation; after operation, large amount of albumen, granular and hyaline casts. Blood cultures: Streptococcus bacteremia. W. B. C. 14,500, 87 per cent. polynuclears. Septic temperature for some time after operation. Recovering; urine now negative.	F	9	5/5	5/5	O. D. Disc swollen and edematous. Veins engorged and tortuous; arteries contracted; slight arteriovenous compression. Retina edematous. O. S. Practically the same as O. D.

SERIES E.

Miscellaneous Retinal. Conditions Suggesting Nephritis	Sex	Age	Vision O D	Vision O S	Ocular Findings.
1. L. F. 3-20-13. Medical Diagnosis: Secondary anemia. Heart: hemic murmur. Urine: Albumen, negative, casts, negative. B. P. 170-180. R. B. C. 3,200,000, W. B. C. 3,900 Hgb. 39 per cent. Has recurrent uterine hemorrhages. Is weak.	F	49	5/6	5/6	O. D. Periarteritis and endarteritis; veins irregular in caliber; arteriovenous compression dilation. Retina hyperemic and edematous; some localized sclerotic retinal changes below macula. Macula edematous. O. S. Sclerotic retinal changes above and below the macula, also nasally. Slight choroidal changes, otherwise does not differ from O. D.
2. J. H. 3-25-13. Medical Diagnosis: Abdominal adhesions, hemorrhoids. Urine: No albumen, no casts. B. P. 155 to 180. Symptoms: Pain in stomach, nausea and vomiting. (Died in hospital).	M	49	5/5	5/5	O. D. Slight periarteritis; slight endarteritis; veins engorged; arteriovenous compression dilation. Few glistening spots in the macula (hyaline, subretinal). O. S. Practically the same as O. D.
3. A. P. 4-12-13. Medical Diagnosis: Reflex vomiting, enlarged tender uterus, right ovary enlarged. Urine: No albumen, no casts. Phenosulphon. elimination rather slow. B. P. 180 to 150. W. B. C. 10,800, R. B. C. 3,930,0000, Hgb. 67 per cent. Symptoms: Dizzy; nausea and vomiting; edema of face and eyelids; voice hoarse; dyspnea at night.	F	48	5/4	5/4	O. D. Retina edematous. Some irregular white spots above the macula; macula edematous. No marked vascular changes. O. S. Arteries slightly contracted; arteriovenous compression dilation. Small white spots in the retina nasally.
4. A. M. B. Medical Diagnosis: Chronic Bronchitis and emphysema of the lungs. Urine negative. B. P. 135. Wassermann negative.	M	75	2/60	2/60	O. D. Lenticular opacities. Disc edematous. Endarteritis; arteriovenous compression. Many exudative spots in the macular area; subhyaloid hemorrhage between the disc and the macula. O. S. Lenticular opacities. Disc edematous. Choric retinal changes in the macula. Retina edematous. Atypical.

Features	Total	%	A Chronic interstitial nephritis	B Chronic Nephritis	C Hypertension	D Acute Nephritis	E Miscellaneous
Total cases	41	100	16....39%	12....29%	7....17%	2.... 5%	4....10%
Male	29	71	13....81%	9....75%	4....57%	1....50%	2....50%
Female	12	29	3....19%	3....25%	5....43%	1....50%	2....50%
Age averages 45			43 to 75-55	24 to 63-45	40 to 78-57	9 to 19-14	48 to 75-55
Vision			c. f. to 5/4	1/60 to 5/4	6/60 to 6/6	5/5 to 5/4	2/60 to 5/4
Opacities of media			1 leucoma 3 cataracts	2 cataracts			1 cataract
Edema of the disc	28		11	7	7	2	1
Congestion or slight swelling of disc	10		3	3	2	2	
Choking of disc I D, or more	7		3	3	1		
Periarteritis	14		3	6	3	1	1
Endarteritis	25		11	6	5		3
Endarteritis of the central artery	1			1			
Irregular, tortuous or contracted arteries	23		9	9	3	1	1
Silver wire arteries	6		5		1		
Cork screw macular vessels	4		1	3			
Arteriovenous compression	10		4	3	1	1	1
Arteriovenous compression dilation	24		8	6	6	1	3
Veins engorged or tortuous	14		1	7	2	2	2
Periphlebitis	3			3			
Venous thrombosis	1				1		
Hemorrhages	21		10	6	4		1
Exudative and other retinal changes	20		11	2	5		2
Edema of the retina	33		14	9	6	1	3
Detached retina	4		1 double 2 1 localized		2 localized		
Edema of macula	23		7	6	7	1	2
Radiating or star shaped macular changes	4		1	3			
Other macular changes	12		4	4	2		2
Choroidal changes	6		3	3			
Choroidal vessels sclerosed	1		1				
Inflammatory characteristics	13		6	5	2		
Atrophic characteristics	6		2	3	1		

Taking up the ophthalmoscopic notes we find that edema was noted twenty-eight times in the disc, thirty-three times in the retina, and twenty-three times in the macula, and that it was found in all the types of the cases examined, though relatively most commonly in interstitial nephritis in which vascular changes are most prominent and nearly as frequently in

the cases of hypertension. Its relation to the blood pressure does not appear, as the B. P. was high in nearly all the cases examined. However, both acute cases show edema and they were cases of low B. P., and edema was present in the case of bronchitis and emphysema in which the B. P. was only 135.

Congestion or slight swelling of the disc was present in ten cases and rather more often in the cases in which elimination was lessened and the blood urea increased. This feature was quite marked when the disc was swollen 1 diopter or more as it was in seven cases.

Of the cases of interstitial nephritis, one disc was swollen one and one-half to two diopters in which the elimination of phenosulphonepthalein was retarded and the blood urea .89 gm. per liter, W. B. C. 8,500, R. B. C. 3,730,000. In the case with the disc swollen two diopters in blood urea was .82 gm. per liter, W. B. C. 5,100, R. B. C. 4,630,000; in the case of swelling of the disc 4 diopters the phenosulphonephthalein elimination was much retarded and the blood urea .72 gm. per liter, W. B. C. 7,750, R. B. C. 4,810,000. All these cases showed considerable albumen and casts. Four other cases of choked disc, papilledema, were found, three in chronic nephritis, and one in hypertension. In the chronic nephritis case in which the disc was swollen four diopters, the phenosulphonepthalein elimination was much retarded, the blood urea .71 gm. per liter, the W. B. C. was 11,200. R. B. C. 3,000,000. In the case swollen 1 diopter and 3 diopters the phenosulphonephthalein elimination was retarded and the blood urea was .68 gm. per liter; the W. B. C. count was 12,700, R. B. C. 4,200,000. In the other case in which the disc was swollen one diopter unfortunately no blood test could be found, but there was no phenosulphonephthalein elimination in two hours. The quantity of albumen was considerable in each case. In the case of hypertension with a swelling of the disc amounting to one diopter the phenosulphonephthalein elimination was retarded, the blood urea not recorded, W. B. C. 9,650, R. B. C. 4,810,000. There has been considerable discussion as to whether choked disc in albuminuria is caused by toxemia or by intracranial pressure. In none of these cases is there a record of increased intracranial pressure but there is a lack of elimination with increase of blood urea in most of the cases. There is no reason why increased intracranial pressure might not be present but it would seem as if the retarded elimination in these cases was of considerable significance.

Periarteritis was present in fourteen cases. It is interesting to note that it was relatively more frequent in chronic nephritis 50 per cent. and acute nephritis 50 per cent. than in interstitial nephritis and hypertension.

Endarteritis is present in twenty-five cases, 61 per cent. It seems to be a more frequent feature in hypertension and interstitial nephritis than in chronic nephritis in which there are six or 50 per cent. The one case of endarteritis of the central artery was probably accidental.

Contracted or tortuous arteries, or arteries with irregularities in caliber are present in twenty-three cases. They are probably associated with the other vascular changes.

Silver wire arteries were seen in six cases of the arterial sclerotic type, five in interstitial nephritis, one in hypertension. They, of course, indicate advanced changes in the vessel walls. They have, when present, some prognostic value.

Corkscrew-like twists in the macular vessels are quite commonly mentioned as indicating sclerotic vascular changes in the retina. When present no doubt they are significant, but they were relatively infrequent, in this series there being but four, nearly 10 per cent.

Arteriovenous compression dilation, in which the venous return flow was so retarded by an overlying artery as to cause the vein to dilate from the increased intravenous tension caused by the compression, was present in twenty-four cases. The condition nearly always shows the presence of increased arterial tension, thickening of the arterial walls, or of both. It may indicate only a local condition, intraocular, but it is usually more or less closely related to a general condition. It may be due to an anomalous condition but in such cases it is not likely to be seen at more than one or two vessel crossings. Changes in the veins other than dilation from compression were relatively infrequent and like periarteritis they were relatively less common in the cases of interstitial nephritis and hypertension.

Hemorrhages were present in ten cases, about 25 per cent. Their diagnostic significance and importance is amply proven. They were relatively more frequent in the cases of interstitial nephritis and hypertension. Exudative changes appear in this series to have the same relation, as to type, as hemorrhages.

That detachment of the retina should be present in 10 per cent. of the cases was a surprise to me, although when one remembers the vascular changes that take place and that these changes may take place in the choroidal vessels also, one can find little difficulty in explaining subretinal fluid which might increase enough to cause a detachment to become extensive. Local detachments have been more frequently noticed, however, and in three of these cases they are localized. All of the detachments are in cases showing vascular lesions predominating, interstitial nephritis two, hypertension two.

The bad prognosis generally given in cases showing radiating or star shaped changes in

the macula is probably justifiable; most cases die within two years; occasionally they live much longer under good care. Rarely these changes are seen in cases presenting no kidney disease. They are caused by exudative and degenerative changes in the retina and their peculiar arrangement is due to the anatomical features of the horizontal layer of Henle.

Other macular changes are often present; their prognostic significance is not nearly as grave. They were present in 29 per cent of the cases. They are seen in cases not albuminuric much more frequently than the star shaped figure.

Choroidal changes were present in six cases, over 14 per cent. They are most likely dependent upon vascular changes in the choroid having the same etiology as the vascular changes in the retina and kidneys. Definite sclerosis of the choroidal vessels was made out in but one case, one of interstitial nephritis.

The thirteen cases showing changes of an inflammatory type include, the cases of choked disc, simple papillitis and exudative retinitis. They all seem to have more or less relation to the rapidity of elimination, the amount of blood urea, and perhaps to the presence of a relative increase in W. B. C., a condition quite noticeable in several of the casse of choked disc.

Atrophic changes are probably common in old cases of all types, or in subacute cases where some of the lesions are old. There were six cases showing such changes, all in the chronic types.

In the acute cases and in the sub acute cases, the changes, other than edema and increased vascular tension of greater or less degree, were relatively small. It is exceedingly interesting to note that practically all the cases showing a rapid elimination also show relatively few retinal changes, and that those changes that do show, are of an early type, without hemorrhages, exudates, sclerotic changes or marked papillitis.

No definite relation could be established between the amount of the blood pressure and the retinal changes; however, the number of cases presented, especially those of the inflammatory or acute types is too small to establish a relation.

In the preliminary considerations in the early portion of this paper the following questions were offered for solution:

1. Is there a recognizable relation between the type of general disease investigated and the associated ophthalmoscopic picture?

2. May there be a definite type of lesion in the central nervous system corresponding to the neuroretinitis, papillitis or vascular changes seen in the retina?

3. Is there a relation between the type of fundus lesion and the type of nephritis with which it is associated?

4. What relation do hemorrhagic and exudative changes in the fundus bear to the pathologic changes present in the acute forms of nephritis?

5. Are there constant characteristic changes in the fundus in cases of parenchymatous nephritis?

6. Can a characteristic relation be established between the vascular changes accompanying chronic interstitial nephritis and the vascular changes in the fundus?

7. Is there any relation between the small dots or spots seen in the macula and the type of vascular change in the fundus?

8. What is the relation between the star like figure in the macula and the type of vascular changes in the fundus?

9. What relation can be established between the pathologic changes found in the fundus in nephritis and the pathologic changes which take place in the several varieties of kidney lesions?

Some of these problems may perhaps be answered more or less satisfactorily while others must be left for another series of investigations, particularly one which shall include a greater variety of cases.

1. Considering the relation between the type of general disease investigated and the ophthalmoscopic picture present, one may refer with advantage to the table on the next page.

Taking up first the cases of interstitial nephritis and the closely related condition hypertension with symptoms similar to those seen in nephritis edema of the retina, disc or macula or some combination of these was present in every case of interstitial nephritis, and in addition, in every case of hypertension. One may conclude, therefore, that edema is a fairly constant ophthalmoscopic finding in nephritis, but, that it is not diagnostic is shown by the fact that it was also present in a high degree in all other types investigated.

Comparing percentages given in the last table we have as predominating features for chronic interstitial nephritis and hypertension, edema 100 per cent., endarteritis 70 per cent., arteries tortuous or contracted 52 per cent., silver wire arteries 26 per cent., arteriovenous compression 61 per cent., hemorrhages 61 per cent., exudative changes 70 per cent., detached retina 17 per cent. In other words the predominating features of chronic interstitial nephritis and hypertension are almost exclusively dependent upon changes in the vascular system, particularly the arteries.

On the other hand we have as predominating features for chronic nephritis, edema 83 per cent, congested nerve head 25 per cent, swelling of disc one diopter or more 25 per cent., periarteritis 50 per cent., endarteritis 50 per cent., arteries tortuous or contracted 75 per cent., cork

Type of Disease / Findings	Edema	Nerve head congested	Nerve head swollen one diopter or more.	Periarteritis	Endarteritis	Arteries tortuous or contracted	Silver wire arteries	Cork screw vessels	Arteriovenous compression	Arteriovenous compression dilation	Veins engorged or tortuous	Periphlebitis	Hemorrhages	Exudative changes	Detached retina	Star shaped macular changes	Other macular changes	Choroidal changes	Changes mostly of inflammatory type	Changes mostly of atrophic type
	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%
A. Chronic Interstitial Nephritis	100	19	19	19	69	56	31	6	25	50	6	0	62	68	12½	6	25	25	37	12
B. Chronic Nephritis	83	25	25	50	50	75	0	25	25	50	58	25	50	17	0	25	33	25	42	25
C. Hypertension	100	29	14	43	71	43	14	0	14	86	29	0	57	71	29	0	29	0	29	14
D. Acute Nephritis	100	100	0	50	0	50	0	0	50	50	0	0	0	0	0	0	0	0	0	0
E. Miscellaneous....	75	0	0	25	75	25	0	0	25	75	50	0	25	50	0	0	50	0	0	0
F. Chronic Interstitial Nephritis and Hypertension combined	100	22	17	26	70	52	26	4	22	61	13	0	61	70	17	4	26	13	35	13

screw vessels 25 per cent., arteriovenous compression 25 per cent., arteriovenous compression dilation 50 per cent., veins engorged or tortuous 58 per cent., periphlebitis 25 per cent., hemorrhages 50 per cent., star shaped macular changes 25 per cent., other macular changes 33 per cent., choroidal changes 25 per cent. The predominating features of chronic nephritis are in the small number of cases presented for comparison somewhat less of a vascular type as regards frequency, although periarteritis was nearly twice as common, and periphlebitis, although presenting but 25 per cent., was entirely absent for the interstitial class. Star shaped macular changes also, in this series are much more frequent in the chronic nephritis class as are to a much less degree other macular changes.

2. The question as to the relation between intracranial conditions and fundus changes cannot be said to have been answered in this series, other than the one instance of hyaline perivascular obliteration to be given further on. That there may have been a relation in the cases of choked disc cannot be denied.

3. The question as to there being a relation between the type of fundus lesions and the type of nephritis present could not be answered without many more cases for comparison. There can be no doubt, however, that if, in this series, one analyzes the observations and deductions derived from the last table, it appears that periphlebitis, tortuous veins, congested or swollen discs and other inflammatory changes with an associated edema of the disc, retina, macula, in over 80 per cent. of the cases, would suggest chronic nephritis, while changes in the intima of the arteries, with edema and other features of high tension and interference with nutrition are more distinctive features in the ophthalmoscopic picture of chronic interstitial nephritis.

The number of cases of acute nephritis is so small that deductions are unsafe although it may not be assuming too much to call attention to the fact that edema, congestion of the discs, periarteritis, tortuous arteries and veins and arteriovenous compression are probably more of an inflammatory or toxic type than of a vascular degenerative type.

The miscellaneous cases seem to show that similar features such as edema 75 per cent., periarteritis 25 per cent., endarteritis 75 per cent., tortuous arteries 25 per cent., arteriovenous compression dilation 75 per cent., veins engorged 50 per cent., hemorrhages 25 per cent., exudative changes 50 per cent., macular changes (not typical) 50 per cent. may be found in conditions not strictly nephritic and that one cannot repose too much confidence in the ophthalmoscopic diagnosis of nephritis.

4. The fourth question must remain unanswered as to acute nephritis, observing in passing, that in so far as our cases go, hemorrhages and exudates were absent in both cases In chronic interstitial nephritis hemorrhages were present 62 per cent. of cases, in hypertension 57 per cent. of cases, combining the two we have for the vascular degenerative type 61 per cent., while in the chronic nephritis 50 per cent. showed hemorrhages. Exudative changes were present in the interstitial type in 68 per cent., in hypertension 71 per cent. or combining as before 70 per cent.; in chronic nephritis exudative changes were present in but 17 per cent. May we conclude from these facts that both hemorrhages and exudates are more characteristic of interstitial than of forms of chronic nephritis not belonging to the class of predominating degenerative arterial changes?

5 and 6. Answers to the fifth and sixth questions insofar as is possible in this series have been included in those already given.

7. The seventh question must not be considered as answered by this series excepting in that macular changes were rather more frequent in the chronic nephritis cases than in interstitial nephritis or hypertension or in the two combined; that macular changes other than edema were absent in acute nephritis and present in 50 per cent. of the miscellaneous cases.

8. Considering question eight one can only say, that while a more or less typical star shaped figure was present in 25 per cent. of the cases of chronic nephritis, this feature was present in but 6 per cent. of the cases of interstitial nephritis and entirely absent for the cases of hypertension. It was also absent in the cases of acute nephritis and from the miscellaneous cases.

9. Question nine is perhaps the most difficult and the most interesting of any. In each case we have an organ made up largely of highly differentiated epithelial cells, differing widely as to embryologic origin, but each bound together by a supporting frame work, and each having a rich and peculiar type of vascular organization and blood supply.[2] As in diseases of the kidney, so in diseases of the retina, the changes which take place are of a degenerative type, often dependent upon the associated or preceding vascular changes.

Edema which was common to all classes and almost constantly present, occurs in the earliest stages of retinitis as a diffuse edema affecting the disc, retina and macula. It gives rise to a watery hazziness or opalescence with increase in the retinal depth as measured by the ophthalmoscopic parallax. Later localized edema may occur in the retinal substance forming cystic spaces which may become filled with hyaline or fat derived from the degenerating arterioles with subsequent formation of cholesterin crystals. When the spaces become large and distended they may rupture externally giving rise to subretinal fluid with detachment. As a result of the pressure edema and intracystic exudate, the nerve elements degenerate, the fluid filling the spaces changes to hyaline, and more or less well defined white spots or areas develop. In the severe types, endothelial leucocytes may penetrate the hyaloid boundary and lead to the formation of white bands, or in more severe cases to proliferating retinitis.

The vascular changes upon which the retinal changes to so large a degree depend are generally the result of hyaline necrosis with fat formation due to changes in the intima. Endarteritis is followed later by deposits of lime salts in the necrotic areas of the intima. The perivascular changes are due, either to albuminous exudate followed by hyaline deposits in the perivascular sheaths, or to a peculiar type of hyaline degeneration seen in other parts of the central nervous system, in which there is deposited around the wall of the artery minute droplets of hyaline which fuse to form a complete sheath for the vessel; the cause of this formation is not known; calcification often occurs.[3] The condition constitutes the true silver wire artery. Hemorrhages when small may undergo complete absorption through the activity of the endothelial leucocytes. If large, the blood pigment may be partially, absorbed through the same means, while fatty degeneration of the coagula followed by cholesterin formation and the development of cystoid spaces with hyaline and other changes, may lead to permanent white patches more or less associated with unabsorbed irregularly arranged blood pigment.

Leaving the retinal side of the picture and turning to the kidney lesions we find, here too, that vascular changes are frequently the predominating feature of the several forms of the disease, with in addition, the peculiar degenerative processes which take place in the various tubules. Here, too, we see hyaline and fatty changes in the vessel walls and in the epithelial cells of the tubules. While amyloid appears in the vessel walls I find no mention of its appearance in retinal disease, however, as amyloid appears to lead to hyaline thickening with gradual occlusion of the vessel lumen, it might be found in the retina also in cases in which an artery becomes obliterated. Amyloid appears first in the glomeruli and the smaller arterioles, and later forms around the tubules, leading to colloid and hyaline degeneration of the epithelium of the tubules.

In the toxic form of acute tubular nephritis marked necrotic changes are seen in the epithelium of the tubes, associated with inflammatory reaction, lymphocyte infiltration, leucocyte migration, etc. Inasmuch as this type of cases was so nearly absent from the series under consideration no retinal relation need be discussed, but inasmuch as similar changes sometimes take place in the heart and liver in toxic conditions, it seems not unlikely that some definite relation may sometime be established.

Toxic glomerular nephritis presents certain peculiar features in which we have (a) the capsular type with inflammatory exudates into the capsular space and degeneration of the capsular epithelium, or in some cases, proliferation of the capsular epithelium; (b) the intracapillary type in which the glomerular capillaries are involved, with intracapillary fibrin formation and the accumulation of leucocytes, without much epithelial involvement. Inasmuch as the types of glomerular nephritis are due to toxins which often have a general distribution and as they are more or less of an inflammatory character

2. Although the choroid is not a part of the retina it is the source of nutrition for the other retinal tissues.

3. Principles of Pathology and Histology, Mallory, P. 444.

one might expect that an associated reaction in the retina would also take on an inflammatory character, as would be shown by neuro retinitis, papillitis, periarteritis, periphlebitis, exudates, etc. In the clinical classification of chronic nephritis in which doubtless there were some cases more or less of these types, inflammatory retinal changes appeared to be predominating features.

In chronic interstitial nephritis, endarteritis affecting the inner fibrous layer and the endothelium, such as occurs in the vessels in general arterial sclerosis, is present. The necrotic process attacks the cells of the intima particularly the fibroblasts, necrosis occurs, and the endothelial leucocytes are set free. When regeneration occurs there is an over production of new elements with consequent narrowing of the vessel. If the endothelial cells degenerate, fibrous thrombi may follow leading to irregular thickening and localized occlusion of the vessel; secondary sclerosis and disappearance of glomeruli follows. When the occlusion is rapid, hemorrhage into the glomeruli may result. The vascular changes are followed by degeneration and atrophy of the renal epithelium with contraction and apparent increase of the connective tissue elements.

That there is quite a definite relation between the pathologic changes in the kidney in interstitial and the associated pathologic changes of albuminuric retinitis would seem to be established in the series by the fact that the retinal lesions recognizable with the opthalmoscope are pathologically as like those found in the kidneys in interstitial nephritis as could be expected in organs so different in function and gross structure.

The preceding report was made possible by the kind co-operation of Professor Albion W. Hewlett and his staff of the Medical Clinic in permitting the use of the cases and in the giving access to their records for the reports on the medical findings. For permission to make the opthalmoscopic studies I am indebted to Professor Walter R. Parker. For kind assistance in collecting the medical notes I am indebted to Dr. D. V. Smith, Assistant in Ophthalmology. I am deeply grateful to all these gentlemen for these kind favors.

DISCUSSION.

Dr. Walter R. Parker: When Dr. Hewlett mentioned to me the fact that on the Medical Clinic they were doing some investigation along the lines of establishing the relationship of the elimination process to the different forms of nephritis, it occurred to me that there was an opportunity for some work along the same lines in connection with the various changes in the fundus. Dr. Slocum was glad to take this phase of the work up and you have heard the report of his investigation.

The investigation of these cases throws us at once into the general problem of vascular-sclerosis with its manifestations. The pathology of the changes in the fundus are no different from similar changes in other parts of the body. They may be local or general, primary or secondary.

The primary form develops apart from any local inflammation, and is seen in chronic alcoholic poisoning, syphilis and albuminuria. The secondary form results from a local inflammation as in disseminated choroiditis or in retinitis pigmentosa. Syphilis may be either the primary or secondary cause of vascular sclerosis. In the second stage when the infection is general with wide spread endarteritis, the sclerosis is primary. But when the disease shows local changes there may be intense local secondary vascular changes.

In general sclerosis as seen in nephritis, there may be a transudation into tissues leading to various changes. If subretinal, we may have detachment. If intraretinal in the nerve fibre layer, gray patches with ill defined margins are seen, if in the internuclear layer, which is the most common form, masses of exudation somewhat star shaped in the macular region are observed. Add to this picture the various forms of hemorrhage as sublyloid, superficial or deep retinal, with the possibility of an embolism of an artery, or a thrombosis of the vein, and you have some idea of the possibilities in a study of this kind. In cases of thrombosis of the central vein, the swelling in the retina and nerve may be so great as to suggest a choked disc as seen in cases of brain tumor, while in interstitial nephritis, the changes may be all limited to the arteries themselves.

I think this study shows that, in general, the cases which have subnormal elimination will show a marked edema, and more swelling, with the consequent changes, than those which have better elimination as in the chronic interstitial type of the diseases where the changes are limited almost entirely to the arteries.

This work will be continued and I hope may add still more to our present knowledge.

Dr. J. H. Agnew: I was very much interested in Dr. Slocum's paper because many of the cases I was observing at the same time in the medical clinic with reference to the urea content of the blood. It is gratifying that Dr. Slocum has been able to group the cases which showed decreased elimination. I think it is very encouraging that there has been some distinct progress made in correlating the fundus findings with the clinical diagnosis.

Dr. C. D. Camp: If I had not already been converted to the use of the ophthalmoscope in the diagnosis of disease, I think Dr. Slocum's numerous and careful observations would convert me. I would call attention, however, to the necessity of not depending too much upon the fundus findings for a diagnosis. This strikes me particularly in reference to the presence of choked disc. You will find that many writers, and I think almost all of the text books make statements that choked disc of two diopters or over is practically pathognomonic of brain tumor. Dr. Slocum found two of four diopters and other cases of between that and two diopters.

Dr. R. Bishop Canfield: I am interested in the case from the clinic of otology because this patient had a suppurative process in the jugular bulb, on account of which the jugular vein and its tributaries were removed. This of course caused considerable decrease in the venous return from the head. It happened that, as is usually the case, the right jugular vein was much larger than the left and at the time of the operation, the venous return was apparently interferred with. The child had two or three diopters of papillary edema. If she

has a diplopia due to involvement of the external rectus of that side, it speaks very strongly for an abscess at the apex of the temporal bone—a very deep seated abscess or a serous meningitis at this point. If this edema can be said to be characteristic of her nephritis it gives greater latitude in attempting to find the cause of her diplopia.

Dr. George Slocum: In the case last spoken of, the condition of the fundus is such as might be found in almost any case of acute nephritis. The changes in the disc and retina were edema, and slight venous tortuosities, and these changes were precisely similar to those in the fundus of the case of acute nephritis in which the etiology was entirely different. The amount of albuminuria and the active change going on in the kidney are entirely sufficient to account for the retinal condition.

311 South State street.

THE PROGNOSTIC VALUE OF A FUNCTIONAL TEST OF KIDNEYS IN PATIENTS REQUIRING PROSTATECTOMY.

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The purpose of this paper is to present briefly tonight a series of cases which although rather incomplete may throw some light upon the prognosis of patients requiring a prostatectomy.

As we all know there has been, and is now considerable discussion as to the technic of a prostatectomy, its after care and its prognosis. Also that few, if any, of the men doing this work are satisfied with their mortality. This paper will only take up the prognostic end of the question.

A few years ago a reagent called phenosulphonephthalein was recommended by Geraghty of Johns Hopkins, for use as a test of renal function. This is purely a color test, one cubic centimeter of the reagent being injected subcutaneously or preferably intramuscularly, the urine secreted during the next two hours then being tested for the amount excreted in that time by comparing its color to that of the standard solution.

Normal kidneys should show the first excretion within ten minutes, and the total excretion for the two hours would be around 75 per cent. Usually the urine of the first and second hours are estimated separately, but in the following cases that has not always been done, as it is very difficult to make a reading if the amount falls below 10 per cent.

The chief cause of death following a prostatectomy is suppression of urine and the subsequent uremic poisoning. In all cases of senile hypertrophy of the prostate there is more or less failure of renal function, due to the back pressure from the never empty bladder, which going up through the ureters acts upon the kidneys with a consequent ill effect upon their function. The object of the functional test is to estimate the degree of damage already done to the kidney and whether their function can be increased up to a point of operative safety.

All cases of senile hypertrophy of the prostate coming into the Hospital, have a permanent catheter placed into the bladder as soon as a diagnosis is made. As soon after this as possible an injection of phenosulphonephthalein is made, and an estimation of their eliminative power is thus made. If this is low, the catheter is kept in place, the object being to keep a constantly empty bladder.

If within a week or two a repetition of the test shows an increased elimination, the kidneys have shown that they can recover, and the prognosis for the recovery of the patient following operation is better. The determination of future procedure depends upon the degree of renal function present. This will be indicated by the following cases.

Case 1. Mr. S., age 80, came into the Hospital before the passing of urine was entirely impossible for him (this is sometimes the case). After a permanent catheter was installed his functional test showed 25 per cent. elimination in the first hour, and 20 per cent. in the second hour. On the strength of this his prognosis was thought to be good, and a prostatectomy was performed within the next few days, the patient having an uneventful recovery.

Case 2. Mr. W., age 67, also came into the Hospital before he was totally unable to void urine, though his trouble was of three years standing. Urinalysis showed albumen, pus, but no casts. His functional test showed a total of 48 per cent. elimination in two hours, so his prognosis was also considered good, and within a week a prostatectomy was performed with an uneventful recovery.

Case 3. Mr. A., age 74, trouble being of two years standing, and for the past five weeks before entrance was unable to pass any urine except by catheter. Urinalysis showed albumen, pus, but no casts. Permanent catheter was installed and the functional test showed 34 per cent. elimination in two hours. The patient stood the catheter very well so it was kept in place for the next two weeks, when another test showed an elimination of 40 per cent. in two hours. This, while not a great increase, yet the fact that there was an increase, made his prognosis rather good, and a week later a prostatectomy was performed with a good recovery.

Case 4. Mr. B., age 61, trouble for four years standing, could pass a little urine, but his residual urine was found to be twelve ounces. Functional test was only 19 per cent. for two hours. A permanent catheter was employed for a week, but as he did not stand it well, a cystotomy was then performed, in an attempt to improve his renal function. At this time a

diverticulum of the bladder was found, situated posteriorly and beyond operative reach. This complication undoubtedly affected his other condition. Five days after the cystotomy his test showed 20 per cent. for two hours. Continuous drainage through the wound and daily irrigation cleared up the cystitis somewhat and about two weeks after the first operation his test showed 23 per cent. elimination in two hours. This, although a very light gain, yet was sufficient to make us think that he stood a good chance, though not the best of recovery, and a prostatectomy was performed. Following this he showed no signs of suppression at any time and went on to an eventual recovery.

CASE 5. Mr. F., age 66, trouble of six years standing, has employed a catheter more or less continually for the past three years. Urinalysis showed albumen, pus, and no casts. Functional test was 41 per cent. in two hours. While this was comparitively good, yet on account of the long continued use of the catheter and subsequent cystitis, it was decided to first perform a cystotomy only. A week after this the functional test was 48 per cent. so a prostatectomy was performed with good recovery.

CASE 6. Mr. S., age 63, trouble of ten years standing, and has used catheter for the past two years. The bladder was very irritable and much inflammed, so much so that he needed catheterization nearly every hour. His urine was loaded with pus, but no casts were found. Functional test showed that ten ounces of urine were secreted in two hours but absolutely no trace of the phenosulphonephthalein could be found. On account of this showing an estimation of the urea content of the patient's blood was made. This was found to be 1.88 grams per 100 cubic centimeters or about four times the normal amount. This confined the previous findings, and made his prognosis very bad. The patient however was unable to stand a permanent catheter, and was suffering more or less continually, so in order to relieve him and on the possibility that he might survive a very short operation under gas anesthesia, a cystotomy was performed. The patient started to secrete urine after operation, although this consisted of little else but water and pus. Within forty-eight hours he developed uremia, and died in uremic coma four days after operation.

CASE 7. Mr. W., age 63, trouble for two years standing, has had to employ a catheter for four months previous to entrance to hospital. During this same period the patient has had rather severe gastrointestinal disturbances, being nauseated and vomiting at frequent intervals. Has been able to take very little nourishment. On entry to Hospital a permanent catheter was installed. Within a few days his nausea and vomiting ceased, and his appetite improved wonderfully. Educational tests on entry was O. Urine was pale, of low specific gravity, had considerable pus, and no casts. Catheter was kept in place and a week later the test was repeated, showing no improvement. Here we have a case of relative, and symptomatic improvement following free drainage of the bladder, but no signs of absolute improvement. After four weeks of treatment with permanent catheter, a cystotomy was performed under local anesthesia. The following day he showed a few beginning symptoms of uremia, but these passed off by the next day, and patient returned to his former condition. Good drainage was maintained through the wound, and two weeks later a functional test was again made, showing absolutely no improvement over the first one. At this same time an estimation of the urea content of his blood showed 3.15 grams per 100 cubic centimeters, or more than six times the normal amount. The patient was then discharged as inoperable. There is no doubt but that a prostatectomy in this case would have been fatal to the patient.

CASE 8. Mr. R. age 80, trouble of ten years standing. For three or four years has had to employ a catheter occasionally. Recently has been unable to get along without one. Patient was in state of chronic uremia on entrance. Urine showed many casts, and much pus. Functional test was 10 per cent. for two hours. The patient would not stand a permanent catheter at all, and on account of his general arteriosclerotic condition, and the condition of his kidneys it was thought that even a cystotomy would be fatal, so the patient was sent home without further treatment.

CASE 9. Mr. S., age 65, is interesting in that it shows a correlation between phenosulphonephthalein test, and the symptomatic condition of the patient. On entry, the test was 37 per cent. for two hours, and the patient was running a slight temperature undoubtedly due to pyelitis. A permanent catheter was installed, and it was thought that within a week or so he would be in condition to be operated. However, at the end of the week the patient developed a subnormal temperature, nausea, loss of appetite, a badly furred tongue and became much weaker.

Shortly after this another test was run, which showed a marked drop down to 20 per cent. in two hours. The patient is now in a state of chronic uremia, and is still in the Hospital, with a permanent catheter, but is considered a very bad operative risk, and such being the case probably no attempt will be made to perform any operation.

There are several more cases which might be reported here, yet as the above have shown nearly every variety of this problem it was decided not to put them in here.

From a study of the above cases the following conclusions may be drawn. First, that the functional test of the kidney is an invaluable aid in determining the prognosis of these cases of senile hypertrophy of the prostate. Second, that when it has been checked up by an estimation of the urea content of the blood, it shows a considerable reliability. Third, that with it as a guide, along with other findings the mortality of these cases could be made very low. Fourth, that it indicates very clearly the affect of back pressure upon the kidney, inasmuch as those that we can call early, show a much better renal function. This would also be a plea for earlier diagnosis, and operative interference as the futility of other methods of treatment and their bad affects has often been demonstrated.

In conclusion I would say that there has been no attempt to compare these findings with those of others, the data being entirely drawn from our own experience during the past six months.

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